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CARDIAC INFARCTION WITH BUNDLE BRANCH BLOCK

BY

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From the Institute of Cardiology, London

Received February 9, 1949

When cardiac infarction is complicated by bundle branch block, the electrocardiogram may or may not show the features characteristic of myocardial injury. Interference with conduction through the left branch of the bundle of His usually suppresses pathological Q waves and other RS–T segment or T wave changes in the standard and unipolar limb leads and in chest leads; it may then be impossible to make a cardiographic diagnosis of cardiac infarction. When a conduction defect involves the right branch, however, cardiographic signs of cardiac infarction can, as a rule, still be recognized (Wilson *et al.*, 1947).

The association of cardiac infarction and bundle branch block is not uncommon (Oppenheimer and Rothschild, 1917; Applebaum and Nicholson, 1935; Comeau *et al.*, 1938; Fischer, 1938; Master *et al.*, 1938; Moia and Acevedo, 1945). Since the majority of these reports were published, the use of multiple chest leads has permitted a higher degree of precision in the diagnosis of cardiac infarction and in the localization of intraventricular conduction defects, and it is likely that in the future the association of these two conditions will be diagnosed more frequently and with greater accuracy (Wilson *et al.*, 1944). The subject is of considerable importance, not only from the viewpoint of practical diagnosis, but also because cardiac infarction complicated by bundle branch block has a mortality almost twice as great as that of infarction with normal intraventricular conduction (Master *et al.*, 1938).

The object of this investigation was to determine the frequency with which the electrocardiographic signs of cardiac infarction could be recongized in the presence of bundle branch block and to discover what factors tended to prevent their suppression.

MATERIAL

The electrocardiograms and case-notes that form the basis of this report were obtained from the records of Hammersmith Hospital, the London Hospital, and the National Heart Hospital. The majority of the patients concerned, however, were examined and investigated by one or other of the writers. A number of patients who had been under observation before the war could not be subsequently traced. Follow-up studies are therefore incomplete.

Generally the diagnosis of cardiac infarction was based on a typical clinical history; when this was lacking, the diagnosis depended on X-ray evidence of ventricular aneurysm or on the demonstration of an infarct at necropsy. Bundle branch block was recognized according to the criteria laid down by Wilson and his co-workers, namely:—

> " . . . when the QRS interval measures 0·12 second or more and the QRS complex in lead I is monophasic and consists of a broad, slurred, flat-topped or bifid deflection, left bundle branch block is usually present. When the QRS interval measures 0·12 second or more and the QRS complex in lead I is biphasic or triphasic and ends with a broad, slurred or notched S deflection the block is usually in the right bundle. When the heart is in the vertical position the limb leads may suggest that right branch block is present when the præcordial curves are characteristic of left branch block, and vice versa. When the QRS interval measures 0·12 second or more and the præcordial electrocardiogram shows some but not all of the features typical of right or left branch block the conduction defect cannot be located with certainty." (Wilson *et al.*, 1944).

RESULTS

The present series consisted of 60 cases of cardiac infarction and bundle branch block, and was divided into two groups depending on whether the electro-

cardiogram revealed evidence of both cardiac infarction and bundle branch block, or of bundle branch block only. The composition of the two groups is presented in Table I.

The main features of the 41 cases showing cardiographic evidence of both cardiac infarction and bundle branch block are set down in Table II.

Cardiac Infarction and Left Bundle Branch Block

There were 33 cases with a clinical history of cardiac infarction and an electrocardiogram showing left bundle branch block. In sixteen of these (48 per cent) the cardiogram also revealed abnormal Q waves, RS–T segment deviations, or altered T waves characteristic of cardiac infarction.

The relative frequency of such signs in the various leads taken are set down in Table III (anterior infarction) and Table IV (posterior infarction).

Anterior Infarction

In experiments on dogs, Wilson and his co-workers have shown that when the left branch of the bundle of His is interrupted, direct leads from the epicardial surface of a left ventricular transmural infarct record the initial positive potential of the left ventricular cavity and therefore cannot show a Q wave. When the infarct includes the ventricular septum, however, the initial negative potential of the endocardial surface of the right ventricle may be transmitted through the infarcted—and hence electrically inert—septum to the cavity of the left ventricle. Then leads facing the left ventricular surface may show an initial negative deflection (Q wave) characteristic of cardiac infarction (Wilson *et al.*, 1944; Sodeman *et al.*, 1944).

In all but one of the 12 cases in which a cardiographic diagnosis of anterior infarction was made, a Q wave was present in lead I and in leads taken over the left præcordium (Fig. 1). A similar change was found in the unipolar left arm lead (VL) in five of the six cases in which it was taken. When present in the left præcordial leads, Q may be expected in leads I and VL, but cannot be guaranteed (Wilson, 1936; Master *et al.*, 1938). Septal infarction was found in all three of our cases of left bundle branch block with a Q in lead I that were examined post-mortem.

RS–T segment deviation in greater or less degree and abnormal T waves usually accompanied abnormal Q waves (Fig. 2); only one example (Case 2) was encountered where a diagnosis of infarction could be made from the RS–T segment or T wave in the absence of a Q wave. Marked RS–T segment elevation and coving is a feature of fresh infarction with left bundle branch block as well as with normal conduction (Bach, 1930; Master *et al.*, 1938; Vela, 1944; Moia and Acevedo, 1945; and others) and has been demonstrated experimentally in animals (Hill, 1934). For a time it may be the only clear sign of infarction, preceding the appearance of Q, or the latter may be indistinct or fail to develop. It follows that if an electrocardiogram can be obtained within a few hours or days of infarction, a cardiographic diagnosis of infarction will be possible in a correspondingly higher proportion of cases despite the left bundle branch block. As a rule, however, the RS–T segment depression in lead I typical of left bundle branch block tends to neutralize the RS–T elevation of anterior infarction, and this segment is usually isoelectric or only slightly elevated or depressed (Fig. 2). RS–T segment elevation is not necessarily confined to the

TABLE I

Electrocardiographic Findings in 60 Cases of Bundle Branch Block with History or other Evidence of Cardiac Infarction

Electrocardiogram	Sex		Age (av.)	Left bundle branch block				Right bundle branch block			
	Male	Female		Ant.	Post.	Ant. and post.	Total	Ant.	Post.	Ant. and post.	Total
Cardiac infarction and bundle br. block (41 cases)	35	6	60	12	4	0	16	14	10	1	25
Bundle br. block only (19 cases)	15	4	63	—	—	—	17	—	—	—	2
Total (60 cases) ..	50	10	61·5	—	—	—	33	—	—	—	27

TABLE II

CASES OF CARDIAC INFARCTION SHOWING ELECTROCARDIOGRAPHIC EVIDENCE OF BOTH CARDIAC INFARCTION AND BUNDLE BRANCH BLOCK

Case No.	Sex	Age	Date of infarct.	Date of electro-cardio-gram	Electrocardiogram					
					Leads taken[2]	QRS (sec.)	Abnormal Q	Deviation of RS–T	Abnor-mal T	Site of infarct at necropsy[3]
					Left Bundle Branch Block: Anterior Infarction					
[1]1	M	60	Indef.	27/1/37	No chest leads	0·44	I		I	Antero-septal
[1]2	M	53	10/11/47	13/11/47	VL, VR, VF V5, V3, V1	0·12		I, III VL V5	I VL V5	
3	F	69	Jan. 1945	5/1/48	CR7–1	0·12	I CR5–2	II CR6–2	I, II CR7–2	
4	F	61	7/5/46	8/5/46	V5, V3, V1	0·12	I V3	V5, V3, V1	I V5, V3	
5	M	60	13/11/46	13/5/47	VL, VR, VF V6–1	0·16	I VL V5	V6–3	I VL	
6	M	73	26/12/46	28/12/46	V5, V3, V1	0·12	I V5, V3, V1	V5, V3	I	
7	M	33	July 1944	4/2/47	VL, VR, VF V5, V3, V1	0·12	I, II VL V5		I, II VL V5	
[1]8	M	40	July 1947	17/11/47	VL, VR, VF V6–1	0·12	I VL V6–5		I VL V6–4	Antero-septal
9	M	57	Indef.	5/4/45	IV R	0·12	I, II IV R		I, II	
[1]10	M	68	(a) 6/4/47[4] (b) 5/10/47 (c) 10/1/48	10/1/48	VL, VR, VF V5, V3, V1	0·12	I VL V5	V5	I	Ant. (recent) Post. (old) 1–V septum (recent and old)
[1]11	M	59	Indef.	10/2/48	V6, IV, V, V2, V1	0·16	I, II V6–5	IVV, V2, V1	I V6	
12	M	45	25/2/48	25/5/48	aVL, aVR, aVF V6–1	0·12	I VL V6–3	I V6–3		
					Left Bundle Branch Block: Posterior Infarction					
16	M	62	Indef.	2/8/46	CR7, CR4	0·12	II, III CR7, CR4	III	III	
17	F	45	23/11/46	27/11/46	V5, V3, V1	0·12	III	III	III	
[1]18	F	59	(a) Aug. '47[4] (b) 20/1/48	22/1/48	VL, VR, VF V5, V3, V1	0·14	II, III VF	I, II, III VL, VF V5[5]	II, III VF	
19	M	60	3/9/47	9/9/47	VL, VR, VF V5, V3, V1	0·12	II, III VF	I, II, III V5[5]	II, III V1[6] VF	
					Right Bundle Branch Block: Anterior Infarction					
[1]20	M	63	(a) Jan. 1946 (b) 25/2/47 (c) 27/2/47	25/2/47	V5, V3, V1	0·12	V5, V3, V1	V5, V3		Antero-septal (recent) Posterior (old)
[1]21	M	81	29/11/47	10/12/47	VL, VR, VF V5, V3, V1	0·12	V3, V1	V3	V5, V3	Antero-septal (recent) Posterior (old)

TABLE II—*continued*

Case No.	Sex	Age	Date of infarct	Date of electro-cardio-gram	Electrocardiogram					
					Leads taken[2]	QRS (sec.)	Abnormal Q	Deviation of RS–T	Abnor-mal T	Site of infarct at necropsy[3]
					Right Bundle Branch Block: Anterior Infarction—continued					
[1]22	M	56	20/12/35	21/12/35	IVR, CR2, CR1	0·16	CR2–1	IV R CR2–1	IV R CR2–1	
[1]23	M	81	Indef.	29/9/46	V5, V3, V1	0·16	I V5, V3, V1	V5	V3	Antero-septal
24	M	79	(a) 3/9/36 (b) Oct. 1936 (c) 14/11/36	15/1/48	VL, VR, VF V6–1	0·16	I VL V6–1	V3–1	V6–1	
25	M	58	Indef.	23/3/44	IV R	0·14	I		I IV R	
26	M	61	May 1937	July 1937	No chest leads	0·12	I		I	
27	M	54	16/5/47	25/9/47	VL, VF V5, V3, V1	0·14	V3, V1		V3, V1	
[1]28	M	59	Indef.	8/4/48	VL, VR, VF V5, V3, V1	0·16	I VL V5, V3, V1	I V5, V3	V3, V1	Antero-septal
29	M	39	24/12/47	6/4/48	VL, VR, VF V5, V3, V1	0·16	I VL V5, V3	VL V5	V5	
[1]30	M	51		5/4/48	aVL, aVR, aVF V7–1, V3R	0·12	aVL V5–1 V3R	I aVL V3		Antero-septal (recent) Posterior (old)
31	M	55	21/4/48	12/5/48	V5, V3, V1	0·12	V1			
32	M	77	10/12/47	13/1/48	VL, VR, VF V6–1	0·16	I VL V5–2			
33	M	63	29/3/48	3/5/48	VL, VR, VF V5, V3, V1	0·16	I VL V5, V3	V3		
					Right Bundle Branch Block: Posterior Infarction					
40	M	61	(a) 1940 (b) 27/7/43	8/1/48	CR7–1	0·16	II, III	II, III	II, III	
41	F	69	Jan. 1938	7/3/38	No chest leads	0·16	II, III	III	II, III	
42	M	51	4/9/46	25/9/46	CR7, CR4, CR1	0·12	II, III	III	III	
43	M	67	Oct. 1947	12/12/47	VL, VR, VF V7–1	0·14	II, III VF	III VF	II, III VF	
44	F	64	(a) Feb. 1946 (b) 28/6/46	9/8/46	CR7, IV R	0·16		II, III	II, III	
45	M	61	Indef.	17/2/41	IV R	0·12	II, III	II, III	II	
[1]46	M	67	(a) May '45 (b) 5/10/47	9/7/45 11/10/47	No chest leads CR7, CR4[7]	0·14 0·12	II, III III	II, III	II, III CR7	
47	M	45	Feb. 1945	18/7/47	CR7, CR3, CR2	0·14	II, III CR7	II, III	II, III	
48	M	54	12/12/47	13/2/48	CR7–1	0·14	II, III	II, III	II, III	
[1]49	M	52	15/3/44	20/3/44	IV R, CF2	0·16	II, III	IV R[8]		Anterior, posterior and septal
50	M	68		24/3/48	VL, VR, VF V6–1	0·12	II, III VF			

[1] Dead. [2] Standard limb leads were taken in all cases. [3] "Anterior" and "Posterior" refer to left ventricle.
[4] Electrocardiogram showed posterior infarction with normal intraventricular conduction.
[5] Marked depression of RS–T segment. [6] Abnormally tall T waves present in lead VI.
[7] Left bundle branch block. [8] In IV R, QRS and RS–T segment indicated involvement of apical region.

TABLE III

ELECTROCARDIOGRAPHIC SIGNS OF ANTERIOR INFARCTION COMPLICATED BY LEFT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
	Standard limb leads (12 cases)	
11	3	11
	Chest leads (10 cases)	
9	8	6
	Unipolar limb leads (6 cases)	
5	1	4

TABLE IV

ELECTROCARDIOGRAPHIC SIGNS OF POSTERIOR INFARCTION COMPLICATED BY LEFT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
	Standard limb leads (4 cases)	
4	4	4
	Chest leads (4 cases)	
1	2	1
	Unipolar limb leads (2 cases)	
2	1	2

acute stages of the infarct but may persist for months or years. In eight of our twelve cases in this group, prominent RS–T elevation in lead I and/or the left chest leads was present for 2 days (Case 10), 9 days (Case 4), 2 weeks (Cases 2 and 6), 2–3 months (Cases 11 and 12), and 6 months (Case 5). In the eighth case conspicuous RS–T segment deviation was still evident in leads CR5–2 three years after the infarct (Fig. 3A) and in Case 11 in leads V4–2 five years after the infarct (Fig. 3B). Persistent RS–T deviation has been described as a sign of cardiac aneurysm (Nordenfelt, 1939; Wilson *et al.*, 1944*b*), but this could not be detected in any of our cases.

Primary T wave changes associated with anterior cardiac infarction usually cannot be recognized in the presence of left bundle branch block, for the latter produces strong T wave inversion in lead I and in leads taken over the left ventricle. In no case did we feel justified in making a diagnosis of cardiac infarction by virtue of T wave changes alone.

Care must be taken in interpreting chest lead curves taken from positions C1 and C2 in uncomplicated left bundle branch block since these leads

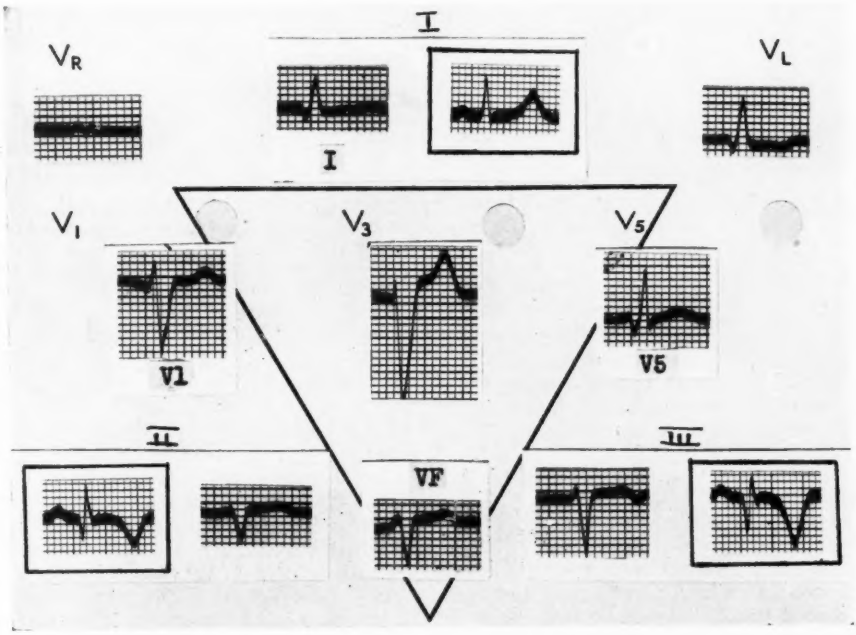


FIG. 1.—Anterior cardiac infarction and left bundle branch block. Previous standard leads, outlined in black, show the original posterior infarct. A prominent Q wave due to involvement of the septum is seen in lead V5, and is transmitted to lead VL and to standard lead I. Autopsy confirmation.

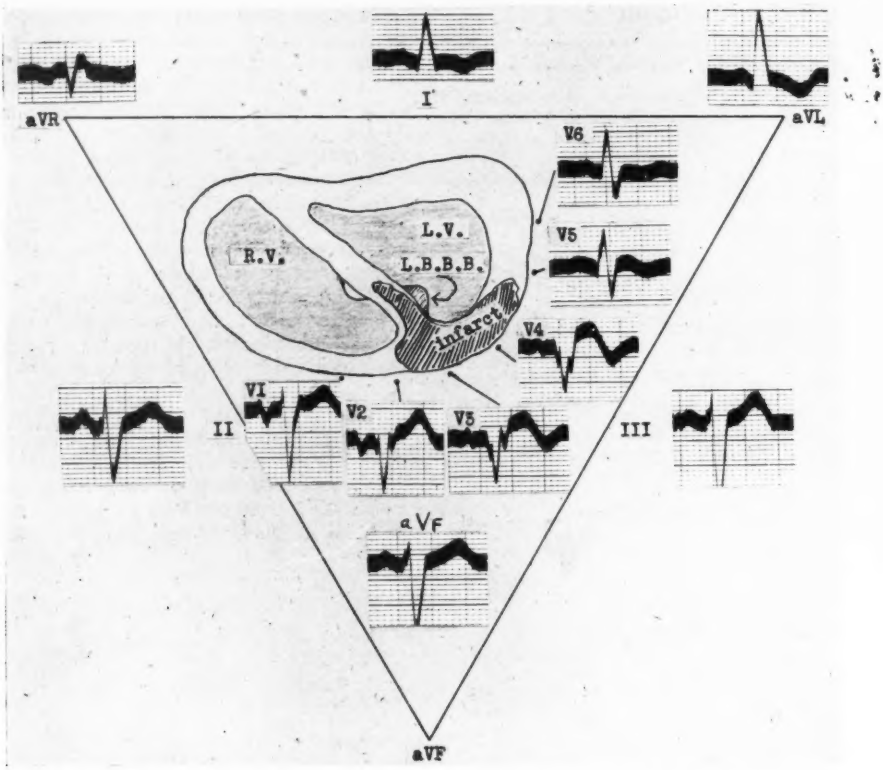


FIG. 2.—Anterior cardiac infarction and left bundle branch block. Elevation of the RS–T segment due to the infarct, seen best in leads V3 and V4, neutralizes any tendency towards RS–T depression due to left bundle branch block: thus in leads VL and standard lead I the RS–T segment is at the isopotential level. The small Q wave in these two leads is due to septal infarction. Autopsy confirmation.

may show an inconspicuous R wave or may consist of a monophasic downward deflection followed by an elevated RS–T segment more or less simulating recent anterior or antero-septal infarction. Such complexes are sometimes known as " false infarction curves " (Mortensen, 1940).

Convincing evidence that left bundle branch block may suppress the signs of infarction was obtained in certain cases in which the block was transient (Fig. 4), or intermittent (Fig. 5).

Cardiographic signs of cardiac infarction obscured by left bundle branch block may be unmasked when a premature ventricular contraction originating on the blocked side allows both ventricles to contract simultaneously. Wilson and Herman (1921) were able to demonstrate the presence of an infarct in the experimental animal by this means and explained the physiological mechanism. We have encountered several examples of this type and others have been reported (Dressler, 1943; Simonson *et al.*, 1945).

Posterior Infarction

When posterior infarction is complicated by left bundle branch block, the appearance of characteristic Q waves depends, as in anterior infarction, on the transmission of the initial negative potential of the right ventricular cavity through an infarcted ventricular septum to the cavity of the left ventricle. This initial negativity is then transmitted through the electrically inert posterior infarct to lead VF, and so to leads II and III. But QIII is also seen in at least one-third of cases of uncomplicated left bundle branch block (Sodeman *et al.*, 1944).

In the four examples of posterior infarction that

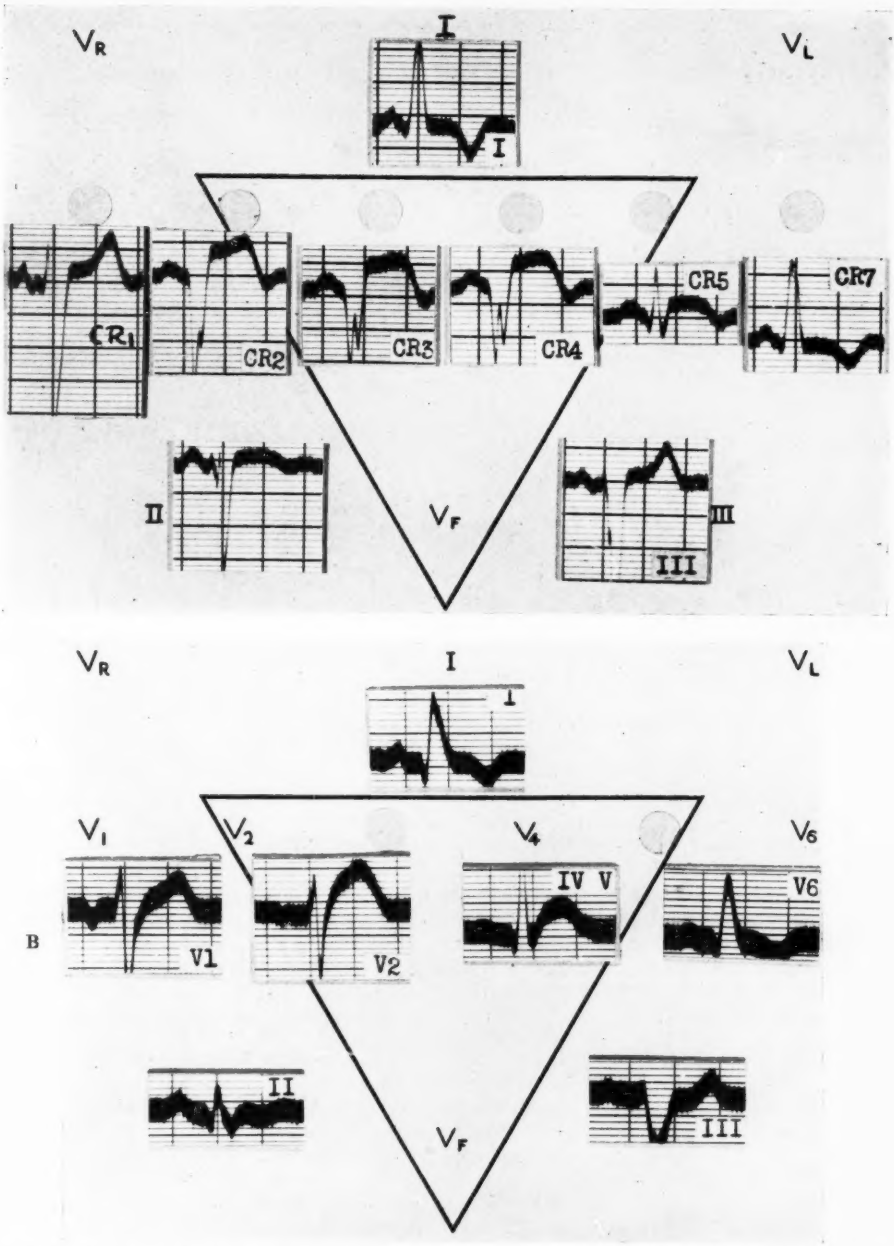


FIG. 3.—Anterior infarct and left bundle branch block showing persistent elevation of the RS–T segment—three years after the infarct in example (A), and five years after the infarct in example (B), best shown in leads CR4 and V4 respectively. The Q wave in left ventricular surface leads or their equivalents in both cases is due to septal infarction.

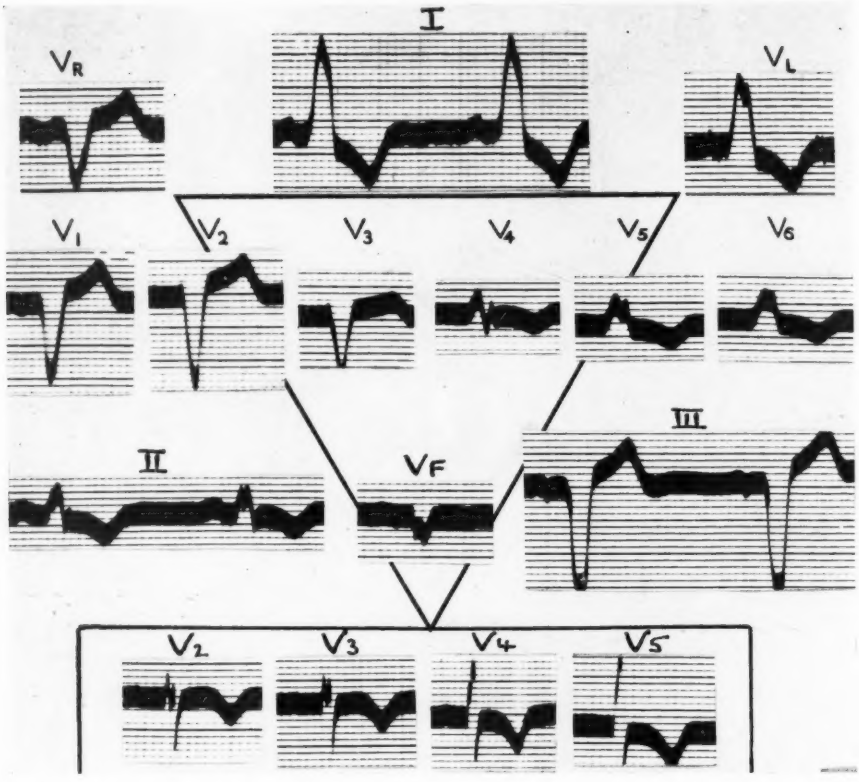


FIG. 4.—Transient left bundle branch block suppressing the signs of anterior cardiac infarction. When conduction was normal (shown below) the T waves were inverted from V2 to V5.

could be diagnosed cardiographically in this series, characteristic Q, RS–T, and T wave changes occurred in lead III. In one instance the curves were taken within a few hours of the onset and revealed RS–T segment elevation in leads II, III, and VF, with reciprocal depression in leads I, VL, and V5 (Fig. 6). Proof of septal involvement in these cases is lacking; three of them recovered, and the fourth did not come to necropsy. On the other hand, extensive posterior infarction not involving the septum was demonstrated at necropsy in Case 75. The cardiogram (standard limb leads and IV R) showed left bundle branch block without the signs of posterior infarction.

Comment

When the different factors are evaluated that tend to permit or suppress the signs of infarction complicated by left bundle branch block, which are discussed below, one may conclude tentatively that in about one-half of such cases cardiographic confirmation of the infarction will be forthcoming; in the other half, as long as the bundle branch block persists, the cardiographic signs of infarction will be suppressed. The diagnosis must then depend on the history and other clinical evidence.

CARDIAC INFARCTION AND RIGHT BUNDLE BRANCH BLOCK

When right bundle branch block is present the sequence of depolarization of the ventricles is the same as when intraventricular conduction is normal. At the start of ventricular excitation the left ventricular cavity is negative and an infarct should transmit this initial negative potential to the surface in the usual way. Therefore the characteristic Q wave of cardiac infarction should not be suppressed.

In our series there were 27 cases of cardiac infarction complicated by right bundle branch block.

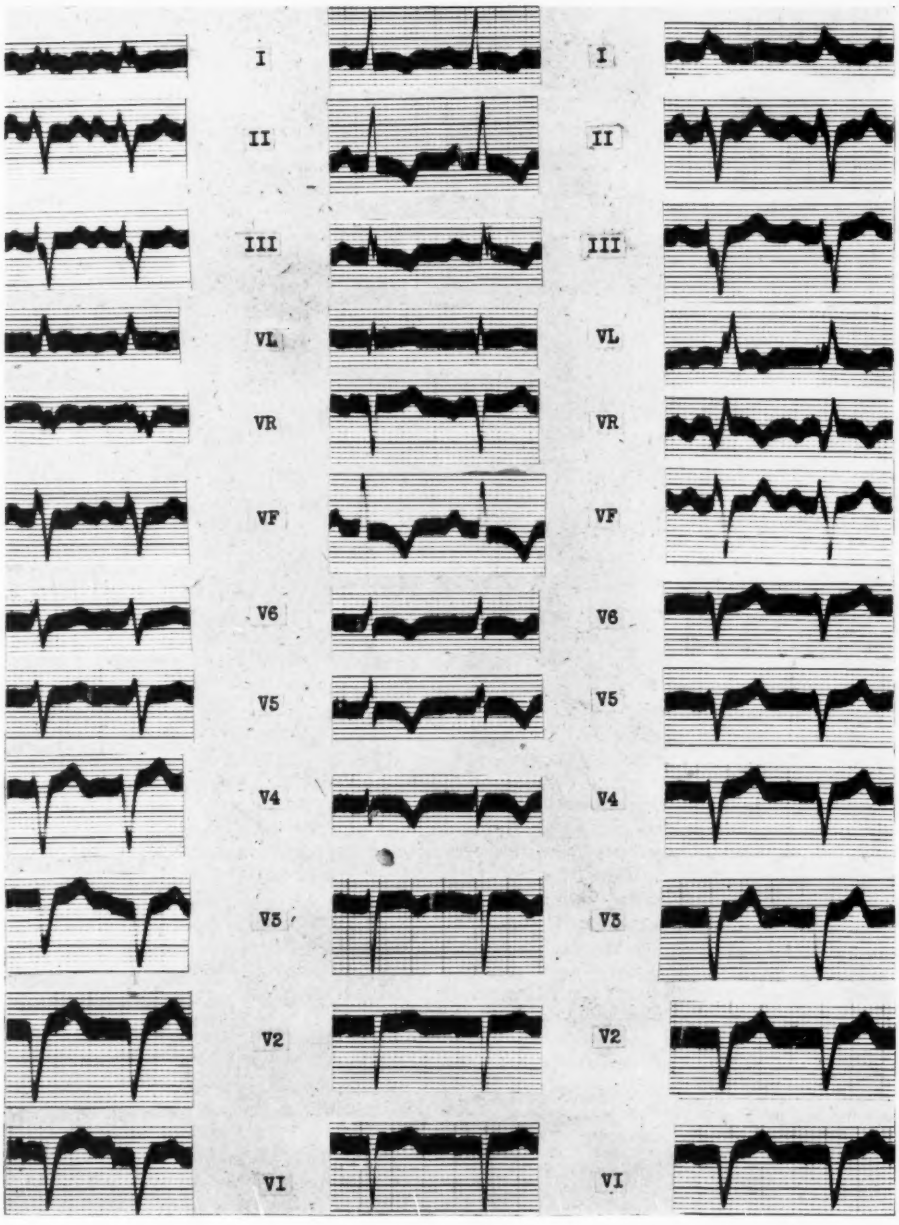


FIG. 5.—Intermittent left bundle branch block (A and C) suppressing the signs of anterior cardiac infarction. When conduction was normal (B), primary T wave inversion of coronary type was seen from V3–V6. As the heart is electrically vertical, this inversion is transmitted to lead VF and hence to all standard leads.

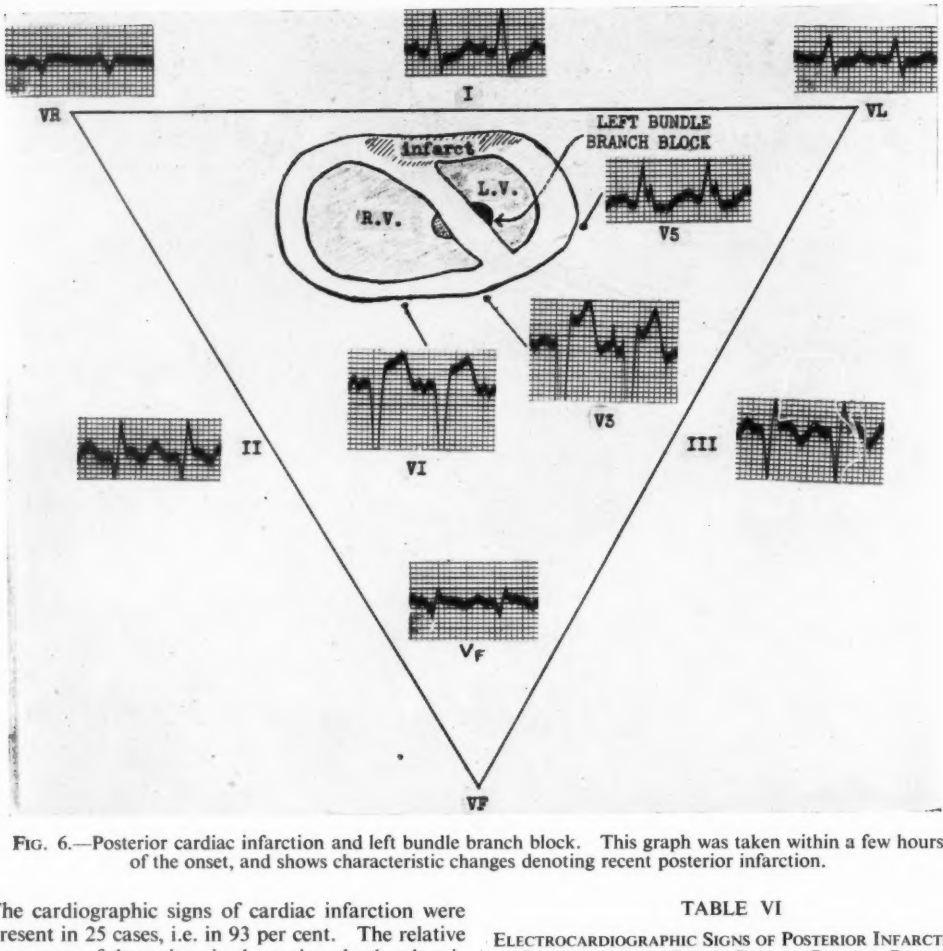


FIG. 6.—Posterior cardiac infarction and left bundle branch block. This graph was taken within a few hours of the onset, and shows characteristic changes denoting recent posterior infarction.

The cardiographic signs of cardiac infarction were present in 25 cases, i.e. in 93 per cent. The relative frequency of these signs in the various leads taken is shown in Table V (anterior infarction) and Table VI (posterior infarction). In six cases the infarct was confirmed at necropsy.

TABLE V

ELECTROCARDIOGRAPHIC SIGNS OF ANTERIOR INFARCTION COMPLICATED BY RIGHT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
	Standard limb leads (14 cases)	
8	2	1
	Chest leads (12 cases)	
12	9	7
	Unipolar limb leads (8 cases)	
6	2	0

TABLE VI

ELECTROCARDIOGRAPHIC SIGNS OF POSTERIOR INFARCTION COMPLICATED BY RIGHT BUNDLE BRANCH BLOCK

Abnormal Q	RS–T Deviation	Abnormal T
	Standard limb leads (11 cases)	
10	9	9
	Chest leads (9 cases)	
1	1	1
	Unipolar limb leads (2 cases)	
2	1	1

ANTERIOR INFARCTION

Eight of the fourteen cases of anterior infarction showed characteristic Q waves in the standard limb leads (Fig. 7). This is contrary to the experience of Wilson *et al.* (1944), Carlotti (1947), and of Goldberger (1947). RS–T segment deviation and

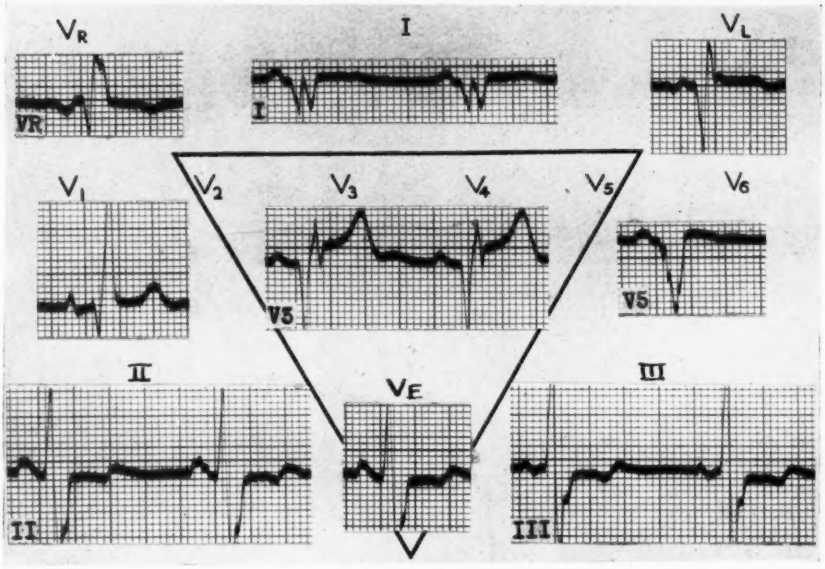


FIG. 7.—Anterior cardiac infarction and right bundle branch block. Typical Q waves are seen in leads V3, V5, VL and standard lead I.

primary T wave changes were commonly absent from the standard limb leads: thus in the six cases showing no Q I, these leads failed absolutely to show the infarct (Fig. 8 and 10).

Multiple chest leads were diagnostic of infarction in the twelve cases in which they were recorded, Q waves being invariably present, and RS–T and T wave changes occurring in the majority (Fig. 9).

The unipolar left arm lead reproduced the Q wave of anterior infarction in six out of eight cases (Fig. 9). RS–T and T wave changes were seldom diagnostic.

In Case 22 (Fig. 10A) no cardiographic evidence of infarction was present six hours after an attack typical of coronary thrombosis. On the following day right bundle branch block (QRS interval measuring 0·16 sec.) had developed; evidence of infarction was then obvious in the chest leads but not in the limb leads. The next record, taken nine days later when normal intraventricular conduction had returned, showed the pattern of anterior or antero-septal infarction in lead I and in the chest leads. Serial cardiograms during the next fourteen months revealed gradual reversion towards normal, but monophasic negative initial ventricular complexes persisted in leads CR2 and CR1.

The cardiogram shown in Fig. 10B was taken a few hours after the onset of a prolonged attack of cardiac pain in a man aged 63 (Case 20) and disclosed right bundle branch block. Diagnostic evidence of extensive anterior infarction was provided by chest leads, but not by limb leads. At necropsy there was a recent infarct involving a large area of the anterior wall of the left ventricle and of the ventricular septum, and an old posterior infarct.

The chest leads in Case 23 (Fig. 11A) showed prominent Q waves in leads V5, V3, and V1, in addition to the features of right bundle branch block. The complex recorded over the right præcordium (V1) resembled that in lead I, while V5 resembled lead III. Therefore, the heart was electrically vertical. At necropsy a recent infarct was found involving the apex and the lower portion of the ventricular septum. The explanation of the tall R waves following deep Q waves seen in chest leads in cases of anterior infarction associated with right bundle branch block is obscure, because as Goldberger has pointed out (1947), the deep Q wave indicates that the lead in question is facing the infarcted left ventricle, whereas the tall R wave ordinarily occurs in leads that face the epicardial surface of the right ventricle in right bundle branch block.

The cardiograms reproduced in Fig. 11B (Case 21) are those of an old man of 81 who developed symptoms of cardiac infarction eleven days previously. The unipolar limb leads showed the heart

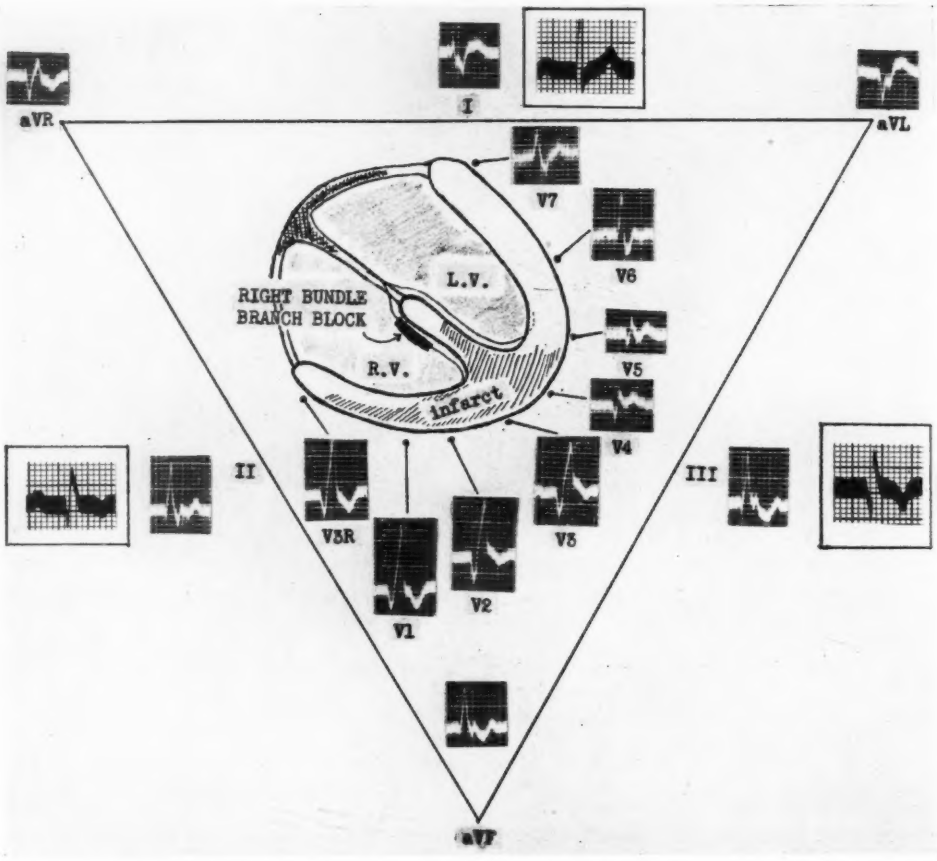


FIG. 8.—Anterior cardiac infarction and right bundle branch block. Typical Q waves are seen in the chest leads, but the standard leads reveal no evidence of the infarct. Standard leads outlined in black were taken previously and represent old posterior infarction. Autopsy confirmation.

to be electrically vertical, and the chest leads pointed to a block in the right bundle branch. Conspicuous deviation of the RS–T segment was seen in lead V3 and small Q waves were present in this lead and in lead V1. The diagnosis was, therefore, right bundle branch block complicating an antero-septal infarct. The patient died a week later and at necropsy this diagnosis was confirmed. In addition an old posterior infarct was demonstrated.

Posterior Infarction

When posterior infarction was associated with right bundle branch block, standard limb leads showed characteristic changes in all 11 cases (Fig. 12). Unipolar limb leads were obtained in only two instances (Cases 43 and 50): lead VF showed significant Q waves in both, with elevation of the RS–T segment and inversion of the T wave in one of them. Multiple chest leads were taken in 9 cases, but revealed evidence of infarction in only one instance.

When the posterior wall of the left ventricle is infarcted, and normal intraventricular conduction is present, the T wave in lead CR7 is usually inverted (Evans and Hunter, 1943). Although there is no apparent reason why a complicating right bundle branch block should suppress the characteristics of posterior infarction in this lead, an upright T wave was present in lead CR7 in five cases, and in V7 in a fourth (Fig. 12 and 13B). The T wave in CR7 was

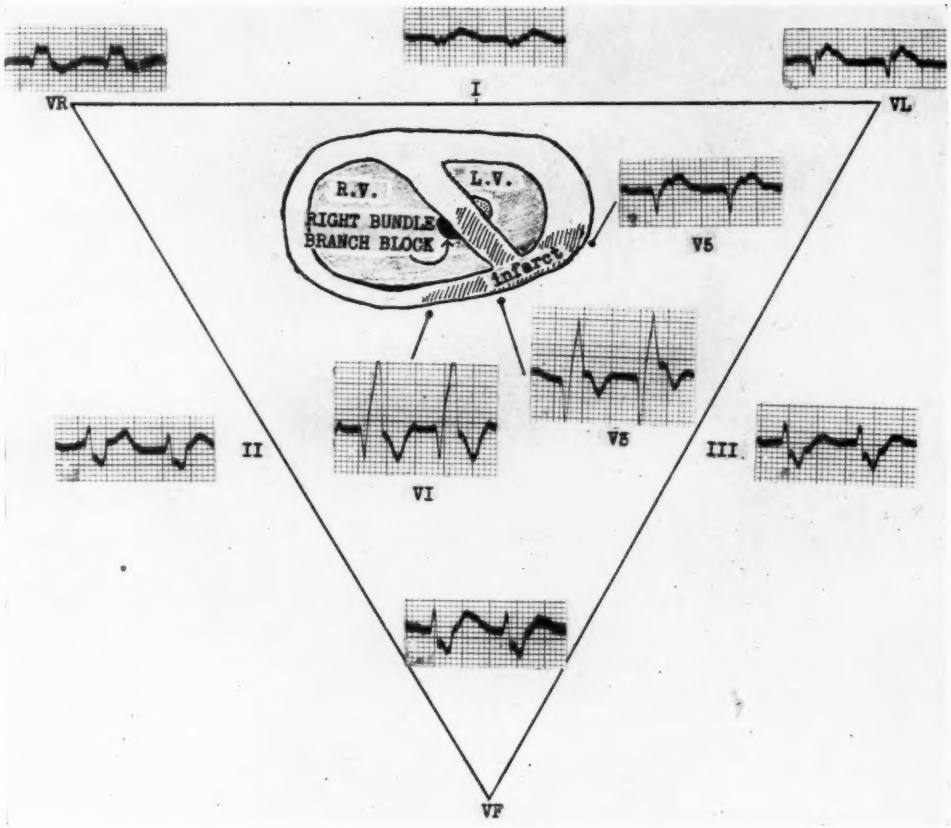


FIG. 9.—Anterior cardiac infarction and right bundle branch block. Characteristic Q waves and RS–T elevation are seen in V3, V5, VL and standard lead I. Autopsy confirmation.

inverted in the fifth case (Fig. 13A). All these records showed indubitable evidence of posterior infarction in other leads.

Some cases with widened and bizarre QRS complexes are the result of fresh infarction distorting the cardiogram of a previous bundle branch block with or without infarction. Alternation of the block between the left and right bundle branches may occur (Master *et al.*, 1938) or the pattern may change permanently from one type of block to another. In this respect Case 46 is of interest. A cardiogram taken in July 1945 showed right bundle branch block with a posterior infarct. Two and a half years later, after another attack of prolonged cardiac pain, from which the patient did not recover, a cardiogram showed left bundle branch block (Fig. 13B). There was no necropsy.

Occasionally, cardiographic evidence of posterior infarction appears to be suppressed by right bundle branch block. This occurred in Case 76, in which the cardiogram showed right bundle branch block with no more than a shallow Q wave in lead III; yet at necropsy the posterior wall of the left ventricle was found to be thinned and fibrosed over a large area. The ventricular septum was not significantly involved. The circumstances that result in suppression of the signs of posterior infarction with right bundle branch block are not clear. We did not feel that a cardiographic diagnosis of infarction could be based on an isolated Q wave in lead III, because this is encountered in 36 per cent of cases of uncomplicated right bundle branch block (Sodeman *et al.*, 1944).

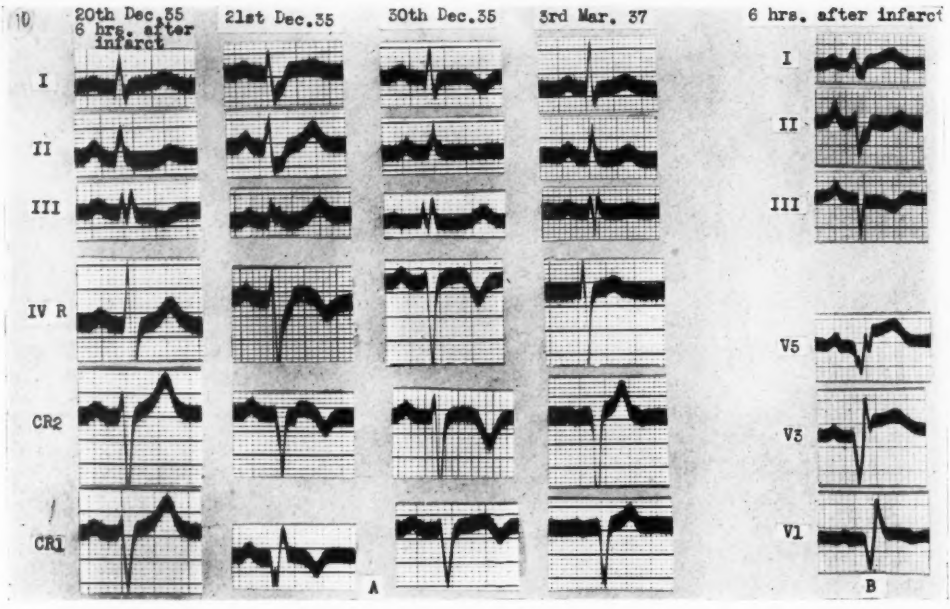


FIG. 10.—Anterior cardiac infarction and right bundle branch block. (A) Serial electrocardiograms showing the development of T wave changes characteristic of anterior infarction: these are masked in standard leads when right bundle branch block is fully developed (December 21). (B) Typical changes of acute anterior infarction are seen in chest leads, but are masked by right bundle branch block in standard leads. Autopsy confirmation.

ANTERIOR AND POSTERIOR CARDIAC INFARCTION COMPLICATED BY BUNDLE BRANCH BLOCK

Necropsy evidence of anterior and posterior cardiac infarction was available in five cases in this series, three of them complicated by right and two by left bundle branch block. In four of them the electrocardiogram showed signs of anterior or antero-septal infarction only; three of these had right (Fig. 8 and 11B), and the fourth left bundle branch block (Fig. 1). The anterior infarct in each of these four cases was recent and the posterior infarct old. In the fifth (Fig. 14) a cardiogram taken six hours after the symptoms of a cardiac infarction showed normal intraventricular conduction with Q waves and depressed S–T segments in leads II and III, and abnormally tall T waves in the chest leads. Five days later, left bundle branch block had developed, as shown in lead CF2; as the heart was vertical, standard leads resemble right bundle branch block. A lead taken over the apex (IV R) was typical of acute anterior infarction. An ante-mortem diagnosis of recent anterior infarction in a vertical heart was made; but at necropsy posterior infarction was also present.

Thus, in these five cases the features of the acute infarct were revealed in the electrocardiogram, and in four of them the signs of an old posterior infarct were suppressed. We have insufficient data, however, to determine the circumstances that result in the dominance of one infarct and the suppression of another.

PATHOGENESIS OF BUNDLE BRANCH BLOCK COMPLICATING CARDIAC INFARCTION WITH AN ACCOUNT OF ELEVEN NECROPSIES

It is reasonable to assume that infarction of the ventricular septum might be associated with bundle branch block because of the intimate anatomical relationship between the septum and the bundle branches. In the experimental animal, septal infarction and usually bundle branch block with or without auriculo-ventricular conduction defects may be produced by ligation of the septal artery or of the left coronary artery (Wilson *et al.*, 1944); but the production of bundle branch block by this technique is sometimes unsuccessful (Barton and Greenwood, 1933). In man the findings are similar. When bundle branch block complicates cardiac infarction

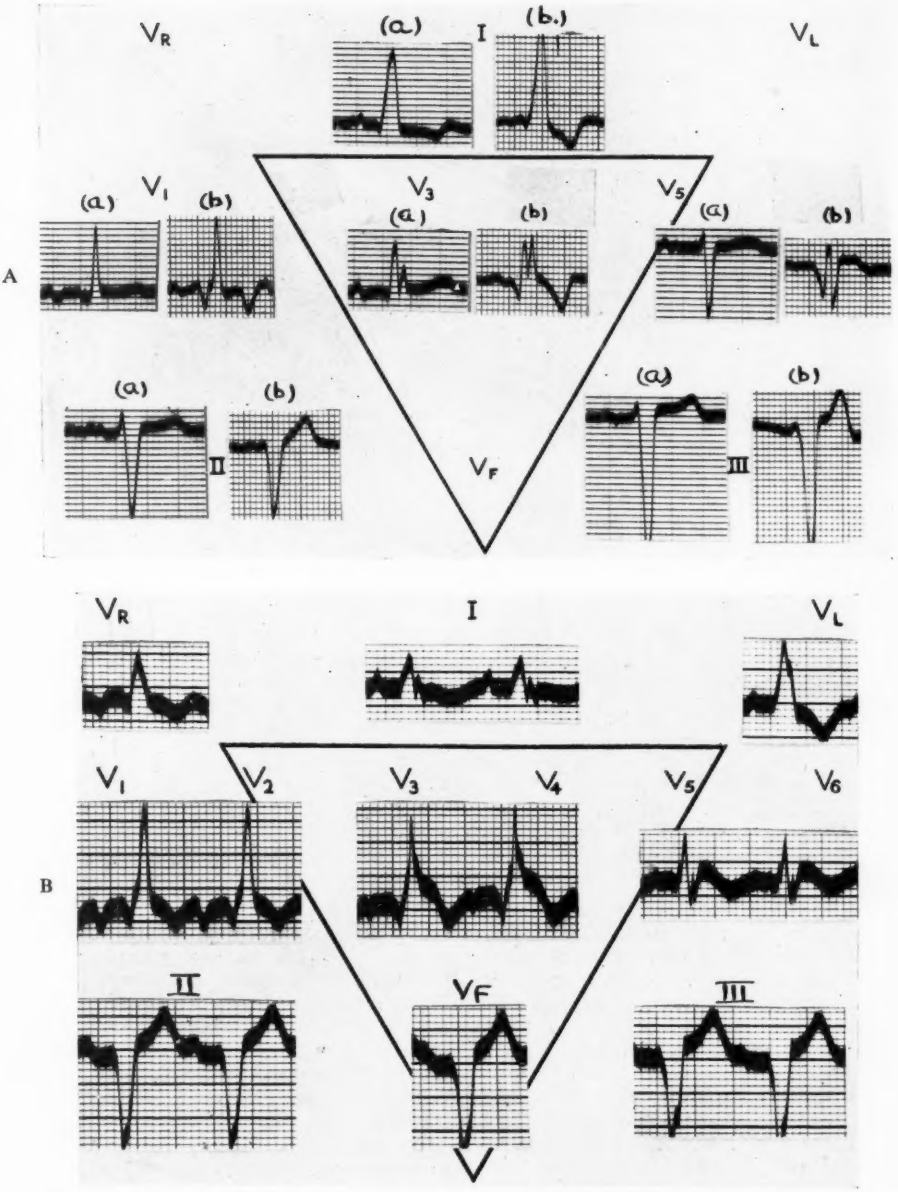


FIG. 11.—Anterior cardiac infarction and right bundle branch block. (A) The control graph (*a*) was taken on 9/9/46, and shows right bundle branch block with a vertical heart. The second curve (*b*) taken on 24/9/46, shows prominent Q waves and inverted T waves in all chest leads due to anterior cardiac infarction. (B) Anterior infarct (11 days old) shown in leads V1 and V3. The right bundle branch block complex in lead V1 is transmitted to lead VL and hence to standard lead I, the heart being electrically vertical. Standard limb leads thus resemble left bundle branch block.

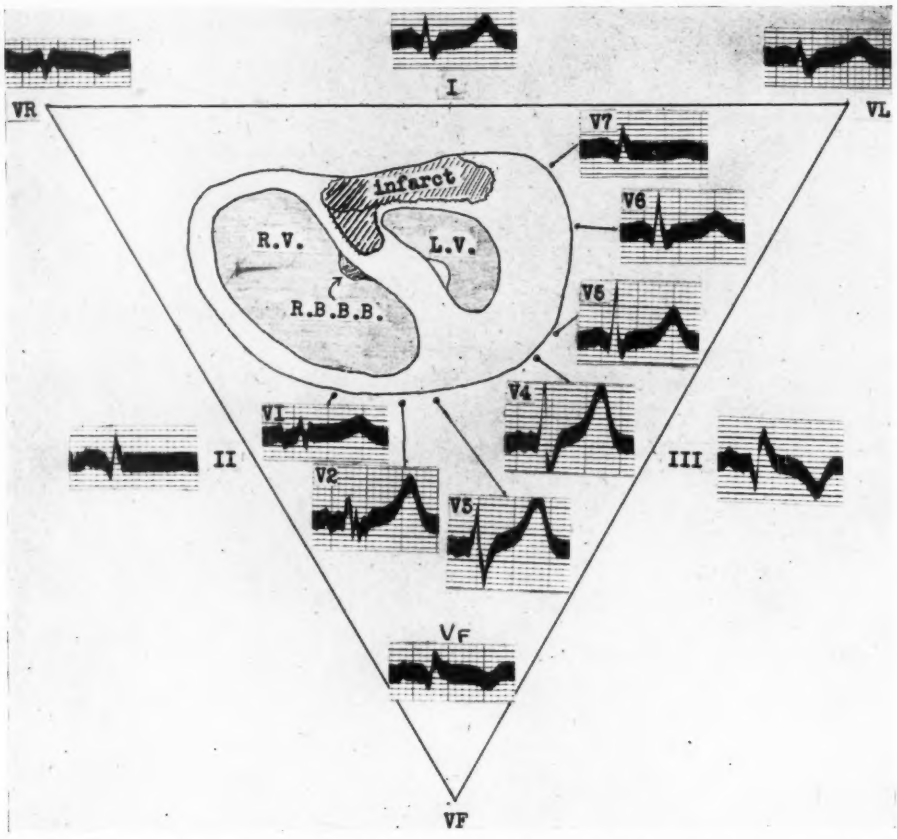


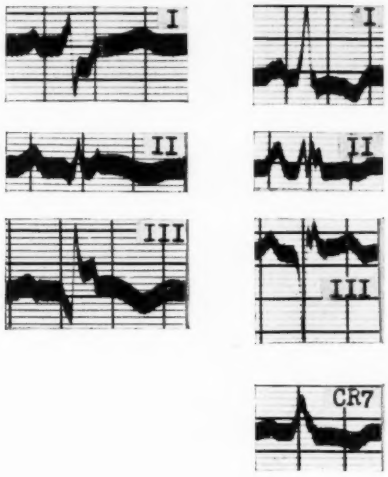
FIG. 12.—Posterior cardiac infarction and right bundle branch block. Pathological Q waves are well seen in lead VF and in standard leads II and III.

the septum is often, but not invariably, involved. In a necropsy study of 30 cases of gross septal infarction, Master *et al.* (1937) found that impaired intraventricular conduction had been present in only 12 cases.

Attempts to correlate the site of coronary occlusion with the occurrence and type of bundle branch block have been reported frequently (White, 1934; Saphir *et al.*, 1935; Applebaum and Nicholson, 1935; Barnes, 1935; Pratsicas, 1936; Fischer, 1938; Master *et al.*, 1938). Applebaum and Nicholson concluded from their necropsy findings in 11 cases that it was impossible to determine which vessel was occluded by the type of block present; for there was usually severe and extensive involvement of the entire coronary system. Master and his co-workers (1938) also submitted that it was impossible to locate the site of an infarct from the type of bundle branch block present. Reviewing their findings in 20 cases examined at necropsy, these authors reported a similar incidence of conduction defects whether the left or right coronary artery was occluded. In 16 of their 20 cases, however, the infarct did involve the septum. When the QRS interval exceeded 0·14 sec. septal infarction was invariable.

The apparent lack of correlation between the situation of coronary occlusion and cardiac infarction, on the one hand, and bundle branch block on the other might be explained by the presence of a gradually developed collateral circulation in the areas supplied by vessels showing long-standing occlusion (Blumgart and Schlesinger, 1940).

There were 11 necropsies in the present series.



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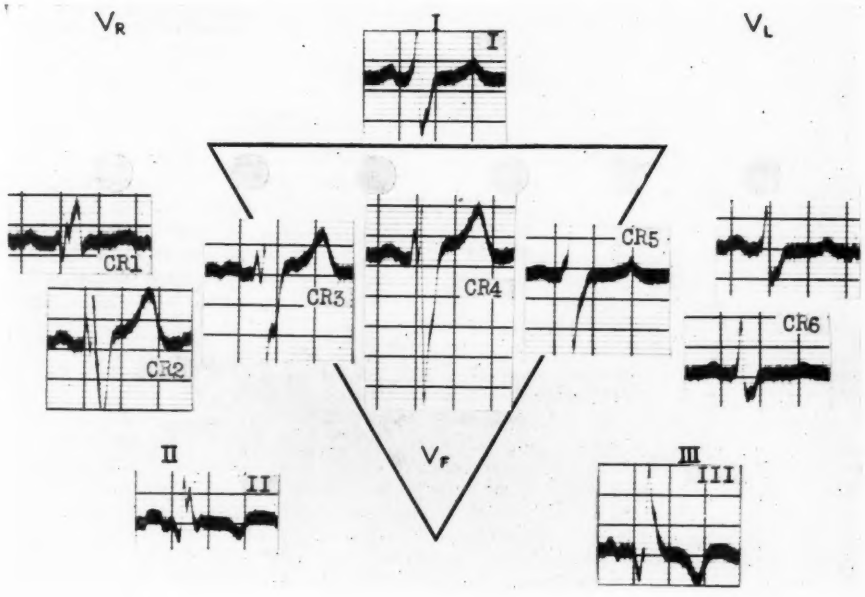

C

FIG. 13.—(A) 9/7/45, showing right bundle branch block and posterior infarction. (B) 11/10/47, showing left bundle branch block after fresh posterior infarction. (C) Posterior cardiac infarction and right bundle branch block. The infarction is shown well in standard leads, but not in lead CR7.

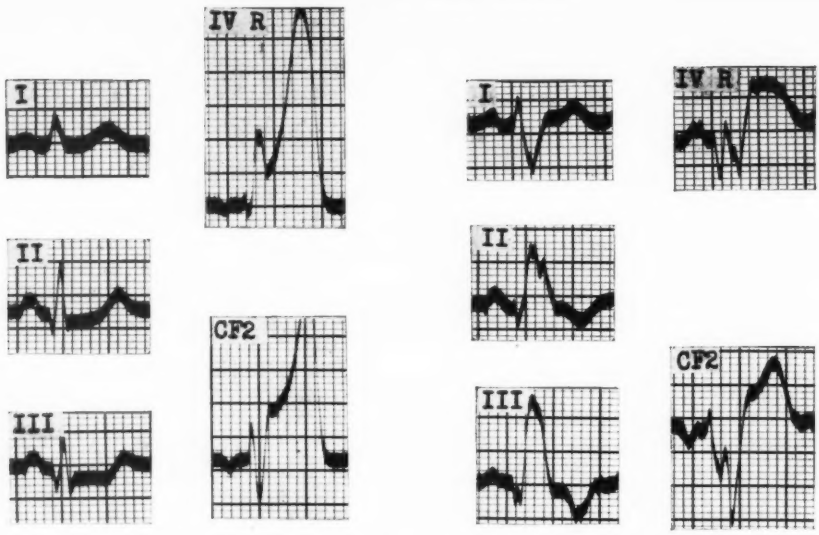

FIG. 14.—Anterior and posterior infarction associated with left bundle branch block in a vertical heart. (A) Normal conduction 6 hours after the onset. Lead 4R shows elevation of the R–T segment and an enormous T wave indicating an anterior infarct a few hours old. The Q wave in leads II and III is derived from lead VF (not shown) to which left ventricular surface potentials are transmitted. (B) 5 days later. Left bundle branch block has developed as shown by lead CF2. The heart being vertical, standard leads resemble right bundle branch block. Changes of acute anterior infarction are shown in lead IVR. Necropsy showed both anterior and posterior infarction.

The main findings, summarized in Table VII, confirm the absence of any clear relationship between the vessel occluded, the bundle branch predominantly involved, and the situation of the infarct.

In 9 cases, however, the infarct involved the ventricular septum. In the 2 instances in which the septum escaped the infarct was situated in the posterior wall of the left ventricle; the electrocardiogram showed left bundle branch block in one (Case 75) and right bundle branch block in the other (Case 76). In 4 of the 9 cases in which the ventricular septum was infarcted, the QRS interval equalled or exceeded 0·14 second.

In a control study we found septal involvement in 58 of 100 unselected cases of cardiac infarction examined at necropsy. From the figures discussed above it is clear that the septum is involved more frequently (80 per cent) when there is bundle branch block. If pathological Q waves occurred in all cases of cardiac infarction, left bundle branch block would not therefore be expected to obscure the pattern in 80 per cent of cases. The actual figure of 48 per cent found in our analysis more or less harmonizes with these expectations, for a minority of infarcts are too shallow to cause Q waves.

SUMMARY AND CONCLUSIONS

Sixty cases with a history or other evidence of cardiac infarction and an electrocardiogram showing bundle branch block have been collected and analysed in order to determine the frequency with which the cardiographic signs of cardiac infarction occur with bundle branch block.

The series comprised 33 examples of left and 27 of right bundle branch block. Cardiographic signs of cardiac infarction were present in 41 cases (68 per cent).

These signs were found in 48 per cent of the cases with left bundle branch block, and in 93 per cent of those with right bundle branch block. As a corollary it should be stressed that the signs of infarction were suppressed in approximately half the cases complicated by left bundle branch block.

The belief that significant Q waves in left ventricular surface leads in cases with left bundle branch block denote septal infarction is supported by limited necropsy evidence.

In the presence of left bundle branch block, the signs of anterior infarction were revealed as frequently with standard limb leads as with multiple

chest leads and unipolar limb leads. In the presence of right bundle branch block, signs of anterior infarction were sometimes seen only in the chest leads.

The signs of posterior infarction were practically confined to the standard limb leads and to lead VF whether the block was in the left or right bundle branch.

TABLE VII

NECROPSY FINDINGS IN ELEVEN CASES OF CARDIAC INFARCTION AND BUNDLE BRANCH BLOCK

Case No.	Electrocardiogram			Necropsy
	QRS (sec.)	Block	Infarct	
1	0·14	Left	Anterior	*Arteries.* Generalized severe atheroma. No thrombosis discovered. *Infarct.* Recent infarction of anterior wall of left ventricle and upper three-quarters of ventricular septum. Fibrosis involving these areas.
8	0·12	Left	Anterior	*Arteries.* Slight atheroma of main vessels. Smaller sub-divisions showed diffuse widespread atheroma. No occlusion. *Infarct.* Anterior wall of left ventricle and ventricular septum. Diffuse fibrosis involving left ventricle and ventricular septum.
10	0·12	Left	Anterior	*Arteries.* Calcified atheroma marked in main arteries. Left anterior descending branch and right coronary completely occluded by organized thrombus. The left circumflex partially occluded by calcified atheroma. *Infarct.* Extensive old infarction of anterior and posterior walls of left ventricle and ventricular septum. Recent infarction involving anterior wall and ventricular septum. Widespread subendocardial fibrosis of left ventricle.
20	0·12	Right	Anterior	*Arteries.* Both right and left coronaries completely occluded and calcified for a distance of 1–2 cm. commencing 2 cm. beyond their origin. *Infarct.* Extensive recent infarction involving postero-inferior two-thirds of ventricular septum, apex and lower one-third of anterior wall of left ventricle. Whole thickness of anterior wall partially necrotic. Old infarction in posterior wall of left ventricle.
21	0·12	Right	Anterior	*Arteries.* Left anterior descending and right coronary arteries occluded. *Infarct.* Recent extensive infarction involving anterior wall of left ventricle and ventricular septum. Old infarction of posterior wall of left ventricle.
23	0·16	Right	Anterior	*Arteries.* Generalized atheroma. Anterior descending branch of left coronary thrombosed in proximal 3 cm.; distal part was laminated and calcified and proximal part fresh and homogeneous. *Infarct.* Apex of left ventricle and lower part of ventricular septum recently infarcted.
28	0·16	Right	Anterior	*Arteries.* Anterior descending branch of left coronary occluded in proximal 2 cm. Left main coronary and circumflex branch normal. Moderate atheroma of right coronary. *Infarct.* Recent infarction of anterior wall of left ventricle and of ventricular septum.
30	0·12	Right	Anterior	*Infarct.* Recent extensive infarction of anterior wall of left ventricle and of ventricular septum. Old fibrosed infarction of posterior wall of left ventricle.
49	0·16	Right	Anterior and Posterior	*Infarct.* Recent infarction of apex and anterior and posterior walls of left ventricle and of ventricular septum.
75	0·12	Left	—	*Arteries.* Marked atheroma of entire coronary tree. Thrombosis of circumflex branch of left coronary. *Infarct.* Large area of posterior wall of left ventricle recently infarcted.
76	0·12	Right	—	*Infarct.* Thinning and fibrosis of old infarction involving posterior wall of left ventricle.

REFERENCES

Applebaum, E., and Nicholson, G. H. B. (1935). *Amer. Heart J.*, **10**, 662.

Bach, F. (1930). *Quart. J. Med.*, **23**, 261.

Barnes, A. R. (1935). *Arch. intern. Med.*, **55**, 457.

Barton, E. M., and Greenwood, H. H. (1933). *Arch. Path.*, **16**, 15.

Blumgart, H. L., and Schlesinger, M. J. (1940). *Amer. Heart J.*, **19**, 1.

Carlotti, J. (1947). *Arch. Mal. Cœur.*, **40**, 99.
Comeau, W. J., Hamilton, J. G. M., and White, P. D. (1938). *Amer. Heart J.*, **15**, 276.
Dressler, W. (1943). *Amer. J. med. Sci.*, **206**, 361.
Evans, W., and Hunter, A. (1943). *Brit. Heart J.*, **5**, 73.
Fischer, R. (1938). *Arch. Mal. Cœur.*, **31**, 997.
Goldberger, E. (1947). *Unipolar Lead Electrocardiography, Philadelphia.*
Hill, I. G. W. (1934). *J. Physiol.*, **81**, 70.
Master, A. M., Dack, S., and Jaffe, H. L. (1938). *Amer. Heart J.*, **16**, 283.
—— (1937). *New York State J. Med.*, **37**, 1707.
Moia, B., and Acevedo, H. J. (1945). *Rev. argent. Cardiol.*, **11**, 341.
Mortensen, V. (1940). *Aet. med. Scand.*, **104**, 267.
Nordenfelt, O. (1939). *Ibid.*, **102**, 101.
Oppenheimer, B. S., and Rothschild, M. A. (1917). *J. Amer. med. Assoc.*, **69**, 429.
Pratsicas, A. (1936). *Arch. Mal. Cœur.*, **29**, 455.
Saphir, O., Priest, W. S., Hamburger, W. W., and Katz, L. N. (1935). *Amer. Heart. J.*, **10**, 567.
Simonson, E., Enzer, N., and Goodman, J. S. (1945). *Amer. J. med. Sci.*, **209**, 349.
Sodeman, W. A., Johnston, F. D., and Wilson, F. N. (1944). *Amer. Heart J.*, **28**, 271.
Vela, M. (1944). *Valor Pronostico del Electrocardiograma, Madrid.*
White, P. D. (1934). *Amer. Heart J.*, **10**, 260.
Wilson, F. N., and Hermann, G. R. (1921). *Heart*, **8**, 229.
——, Johnston, F. D., Hill, I. G. W., Macleod, A. G., and Barker, P. S. (1934*a*). *Amer. Heart J.*, **9**, 459.
—— (1936). *The Electrocardiogram in Diseases of the Coronary Arteries* in *Diseases of the Coronary Arteries and Cardiac Pain.* (Robert Levy.) New York.
——, Hill, I. G. W., and Johnston, F. D. (1934*b*). *Amer. Heart J.*, **9**, 596.
——, Johnston, F. D., Rosenbaum, F. F., Erlanger, H., Kossmann, C. E., Hecht, H., Cotrim, N., De Oliveira, R. M., Scarsi, R., and Barker, P. S. (1944). *Amer. Heart J.*, **27**, 19.
——, Rosenbaum, F. F., and Johnston, F. D. (1947). *Advances in Internal Medicine*, vol. 2, New York.

AORTIC SINUS ANEURYSMS

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The three slight dilatations of the aorta immediately above the corresponding valve cusps, known as the aortic sinuses of Valsalva, are almost entirely intracardiac and lie near important parts of the heart (Fig. 1). Aneurysms arising from these sinuses may extend into the cardiac chambers and encroach upon the pulmonary valve, the atrioventricular valves, the conducting bundle, or the pulmonary or coronary arteries, or may lead to aortic regurgitation by deforming the aortic ring. They may rupture into one of the cardiac chambers, the pulmonary artery, or the pericardium, and sometimes communicate from birth with a cardiac chamber or the pulmonary artery. To these various complications such aneurysms owe much of their interest.

Aneurysms confined to the aortic sinuses are uncommon; Smith (1914) noted that in 8138 necropsies only 7 were found and, in all, only 20 cases were confirmed at necropsy prior to 1914. These aneurysms may be due to any of the usual causes, but those of congenital origin are of particular interest. The first recorded case of this type appears to be that of Thurnam (1840) and when Abbott (1936) collected her 1000 cases of congenital heart disease she was able to find only 12 congenital aortic sinus aneurysms recorded (Bauer & Astbury, 1944).

Our objects in this paper are to describe four new cases, which present certain features of interest, and to review the available clinical and pathological material particularly so far as it illustrates the pathological differences between the acquired and congenital types of aneurysm or aids the clinical diagnosis of congenital aneurysms. Some preliminary discussion of the nomenclature of the aortic sinuses and of the topography of the aortic root is desirable to clarify the anatomical features of the cases to be described.

Nomenclature of the Aortic Sinuses

The many ways of naming the aortic cusps and their sinuses are so confusing that it is often difficult to identify the sinus described. In Table I we have enumerated five methods of nomenclature and in Fig. 2 have indicated the sinus to which each name refers. The standard nomenclatures [Old Terminology; Basle Anatomical Nomenclature, 1895 (B.N.A.); Birmingham Revision, 1933 (B.R.)] have assumed that one aortic sinus lies anterior and two posterior, and always placed in an anterior position the sinus from which the right coronary artery arises, but Walmsley (1929) has pointed out that sometimes two aortic sinuses lie anterior, and one posterior (Fig. 2); he suggested that sinuses related to the coronary arteries should be named right and left coronary sinuses, the third sinus being called the non-coronary sinus. This nomenclature is easy to understand and allows the sinuses to be named when the heart has been removed from the body and the sinuses exposed by opening the aorta; we have therefore adopted it in this paper.

Topography of the Aortic Root

The structures adjacent to the aortic sinuses are of considerable importance in discussing the clinical and pathological features of sinus aneurysms; these structures are illustrated in Fig. 1 and described in the caption.

The annulus fibrosus. Between the aorta proper and the main body of the left ventricle there is a tubular zone of fibrous tissue, the annulus fibrosus, which forms an important part of the wall of the aortic sinuses and extends downward to become incorporated in the aortic vestibule of the left ventricle. It is believed that congenital sinus aneurysms arise from defective development of the bulbar septum which divides the primitive exit

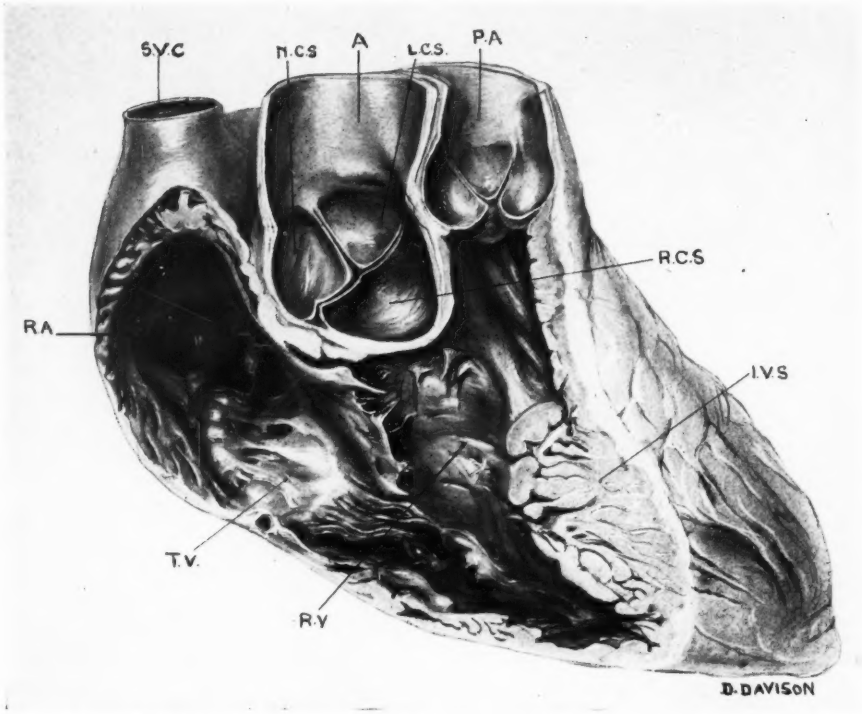

FIG. 1.—*Position of the aortic sinuses.* From a normal heart, fixed unopened, with vessels and chambers distended. The anterior and part of the right walls of the right ventricle and right auricle have been removed and the aorta opened. The anterior part of the ventricular septum (I.V.S.) has been sectioned. The right coronary sinus (R.C.S.) projects into the conus of the right ventricle (R.V.). The non-coronary sinus (N.C.S.) projects into the right auricle (R.A.) and the tricuspid valve lies below adjacent sectors of the non-coronary and right coronary sinuses. The left coronary sinus (L.C.S.) with its coronary artery can be seen postero-laterally. It is related behind to the mitral valve and the left auricle. S.V.C.—Superior vena cava. A.—Aorta. P.A.—Pulmonary artery.

tube of the heart, the bulbus cordis, into right and left halves. Since the annulus fibrosus arises from the bulbus cordis and forms part of the wall of the aortic sinuses, it is a particularly important structure to study when a sinus aneurysm is present.

CASE REPORTS

Case 1. *A congenital aneurysm of the right coronary sinus associated with a bulbar ventricular septal defect, clinically simulating patency of the ductus arteriosus and complicated by subacute bacterial endocarditis.*

In April, 1939, a schoolboy, age 12, was referred to Dr. Crighton Bramwell on account of a heart murmur first discovered during a respiratory infection in infancy. Apart from tonsillitis when 5, he had enjoyed good health. At school he led a normal life and played games, including football, without cyanosis or unusual dyspnœa. At 10 years of age tonsillectomy was advised, but not performed owing to the cardiac murmur. He suffered from epistaxis on several occasions and in August and December, 1938, severe attacks occurred.

On examination his general development was normal; height 60 inches, weight 80 lb. His exercise tolerance was good and there was no cyanosis or finger clubbing. The pulse was regular, rate 80, the blood pressure 125/40. To the left of the sternum, at the base, systolic and diastolic murmurs were heard. Cardioscopy showed considerable enlargement of both ventricles, but a cardiogram was normal apart from R waves of

TABLE I

NOMENCLATURE OF THE AORTIC SINUSES

	Walmsley (1929)	Common position		Less common position	
	(*a*)	(*b*) B.R. 1933	(*c*) B.N.A. 1895	(*d*)	(*e*)
1	Right coronary	Anterior	Anterior	Right	Right anterior
2	Non-coronary	Right	Right posterior	Posterior	Posterior
3	Left coronary	Left	Left posterior	Left	Left anterior

exceptionally high voltage in the standard limb leads. The condition was diagnosed as patency of the ductus arteriosus.

In January, 1942, subacute bacterial endocarditis was suspected and he was admitted to hospital. Seven weeks prior to admission he had a pyrexial illness lasting a few days accompanied by vomiting and shivering. Subsequently his appetite failed to return and he complained of transient pains in the limbs, felt continually tired, lost weight, and was troubled by nocturnal sweating. For a week before admission he suffered from substernal pain which frequently awakened him at night.

On examination he weighed only 84 lb. and was pale. His temperature was 100·2° F. Striking arterial pulsation was visible in the neck, the pulse was regular, rate 120; the blood pressure 120/30. A systolic thrill was palpable in the second and third left interspaces near the sternum accompanied by a harsh systolic murmur and a softer diastolic murmur, both maximal in the same position, but audible over the whole præcordium. A teleradiogram showed considerable cardiac enlargement (cardiothoracic ratio 0·66) involving both ventricles. The cardiogram was similar to the previous record. The liver was palpable two inches below the costal margin; there was no œdema but a few moist sounds were heard at the lung bases. The spleen was palpable and there were scattered petechiæ on the abdomen, chest, neck, and arms. An Osler's node was found on the tip of the right little finger. Blood culture yielded a growth of *Streptococcus viridans*. His condition steadily deteriorated and three weeks after admission he collapsed suddenly and died the following day.

At *necropsy* a few petechiæ were found on the arms; there was subcutaneous œdema of the trunk and effusions were present in the pericardial, pleural, and abdominal cavities. There was generalized passive congestion and infarcts were present in the spleen and right lung; these appearances were confirmed histologically.

The *heart* was globular in shape and weighed 600 g. The right atrium was slightly hypertrophied but the left was normal. The right ventricle was slightly, and the left ventricle considerably hyper-

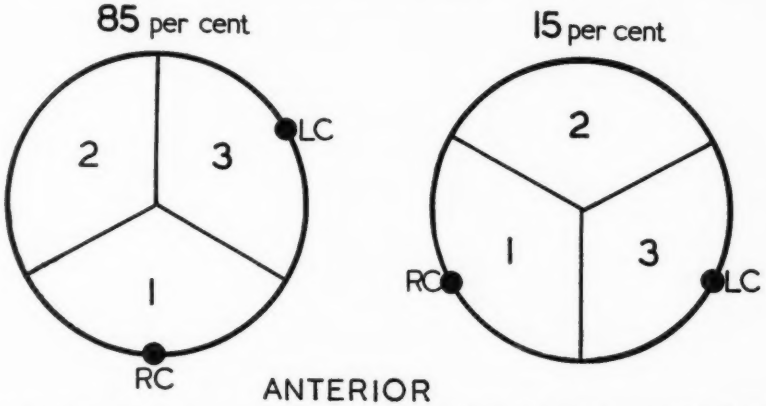

FIG. 2.—*Nomenclature of the aortic sinuses.* (1), (2), and (3) are the sinuses named in Table I. R.C.—right coronary artery. L.C.—left coronary artery. The percentages refer to Walmsley's (1929) estimate of the relative frequency of the two arrangements.

trophied. The foramen ovale and the ductus arteriosus were closed. In the anterior part of the ventricular septum, immediately below the right coronary cusp, there was a triangular opening, base 1·3 cm., height 0·8 cm., communicating between the conus of the right ventricle and the aortic vestibule of the left ventricle (Fig. 3). This opening lay anterior to the membranous septum and above the septal and parietal muscle bundles; it was therefore a defect of the true bulbar septum. Vegetations characteristic of subacute bacterial endocarditis were present around the margins of the septal defect.

The right coronary sinus was enlarged to form an aneurysm with a mouth 2 by 2 cm. and a depth of 2·5 cm. From the upper limit of the mouth the wall of the aneurysm extended horizontally for a distance of 0·6 cm., and then curved downwards obliquely for 0·5 cm. to a well defined transverse ridge. Below this the outer wall of the aneurysm was related to the muscle of the right ventricle and then joined the right coronary cusp. The size of the right coronary cusp was about normal but, owing to the aneurysm, the intercommissural distance was small; consequently the cusp sagged downwards through the septal defect (Fig. 3A), its lower part forming the upper margin of the communication between the ventricles. This sagging

FIG. 3.—*Case* 1. *From a drawing of the aneurysm.* (*A*) *Aortic and left ventricular aspect.* (*a*)—The aneurysm. The sagging of the right coronary cusp can be seen. The arrows indicate the margins of the ventricular septal defect, which is surrounded by the vegetations of bacterial endocarditis. (*B*) *Pulmonary and right ventricular aspect.* (*b*) The apex of the aneurysm projecting into the right ventricle through the septal defect. The margins of the septal defect are indicated by arrows.

had made apposition of the aortic cusps impossible so that the valve was incompetent.

The non-coronary aortic cusp was enlarged, measuring 3 cm. between the commissures and the corresponding sinus was deeper than usual (1·9 cm.). The left coronary cusp measured 1·5 cm. between the commissures. The right coronary artery was much smaller than the left, its orifice lying in the part of the aneurysm adjacent to the non-coronary sinus. The left coronary orifice was puckered and lay near the commissure between its sinus and the non-coronary sinus.

On *histological examination* the aorta and aortic valve cusps were normal apart from the vegetations and the inflammatory changes of bacterial endocarditis. From the annulus fibrosus a tongue of fibrous tissue ran upwards to the transverse ridge on the aneurysm wall, lying between the muscle of the right ventricle and the endothelial lining of the aneurysm. The aortic media terminated at the transverse ridge.

In addition to the aneurysm, several congenital anomalies were present; a bulbar septal defect, an abnormal tongue of fibrous tissue arising from the annulus, and grossly unequal aortic cusps. The aortic wall was free from disease other than bacterial endocarditis, which might have arisen upon the developmental defects. In view of these findings, it seems justifiable to attribute the aneurysm to a developmental anomaly.

The presence of aortic incompetence accounted for the collapsing pulse, the large pulse pressure, and the diastolic component of the murmur. The systolic component and the thrill were explicable by the presence of the ventricular septal defect.

Case 2. *A congenital aneurysm of the right coronary sinus, which ruptured into the conus of the right ventricle and led to progressive heart failure.*

In January, 1944, a man of 41, a chauffeur, was admitted to hospital, complaining of breathlessness and swelling of the legs and abdomen. Heart disease was first found at the age of 24 when he had a severe attack of breathlessness and præcordial pain. From that time he suffered from dyspnœa on exertion and præcordial pain. Some weeks before admission he noticed swelling of the legs and abdomen and his dyspnœa became more severe. He had never had rheumatic fever nor chorea and cyanosis had not occurred in childhood.

On examination he was cyanosed, dyspnœic at rest, and the neck veins were engorged. The pulse was regular, rate 104 a minute; systolic blood pressure 140 mm., diastolic end-point uncertain, the sounds being audible to complete decompression. The heart was enlarged, and a coarse systolic thrill was palpable over the whole præcordium, most intense in the third left interspace near the sternum. Very loud, coarse, systolic and diastolic murmurs of machinery type were audible over the whole præcordium, but best heard in the third left interspace near the sternum. The liver was enlarged and tender and free fluid was present in the abdomen. There was considerable œdema of the legs and sacral area.

A cardiogram showed left axis deviation with depression of the RS–T segments in leads I and II; these appearances were attributed to left ventricular enlargement. A teleradiogram revealed considerable cardiac enlargement (cardio-thoracic ratio 0·63) involving both ventricles, but principally the left. The pulmonary artery and the pulmonary vascular markings were prominent.

With treatment by rest, mercurial diuretics, and digitalis he gradually improved, but his œdema did not entirely disappear. During his fourth week in hospital his condition began to deteriorate, his œdema increased, he became very breathless, and was soon jaundiced and pyrexial; he died after four weeks in hospital.

Necropsy was performed by Dr. G. Stewart Smith. The skin and mucous membranes were jaundiced and there was some œdema of the legs. The whole upper lobe of the right lung was consolidated and typical of the stage of grey hepatization of lobar pneumonia. Both lungs were congested and œdematous. There was generalized chronic venous congestion.

The *heart*, which we examined, weighed 640 g. In the left half of the right coronary sinus there was a round opening 0·7 cm. in diameter with rounded, slightly irregular margins (Fig. 4B). This led to a globular thin-walled cavity (Fig. 4A), 2 cm. in diameter, which projected into the conus of the right ventricle between the septal (posterior) and right anterior cusps of the pulmonary valve (Fig. 4A). On the upper surface of the aneurysmal sac was an aperture approximately rectangular in shape, 0·8 cm. by 0·6 cm., with smooth, rounded and thickened edges. The irregular shape of this opening suggested that it was due to rupture of the aneurysm and, since the edges were smooth and rounded, healing had occurred. The aneurysm thus formed a communication between the aorta and the right ventricle. The right coronary artery arose near the commissure between its sinus and the non-coronary sinus (Fig. 4B).

In the outflow tract of the left ventricle, 0·5 cm. below the aortic valve, was a fibrous band, lying on the interventricular septum, and extending from the right upper margin to the left upper margin of the anterior curtain of the mitral valve (Fig. 4B).

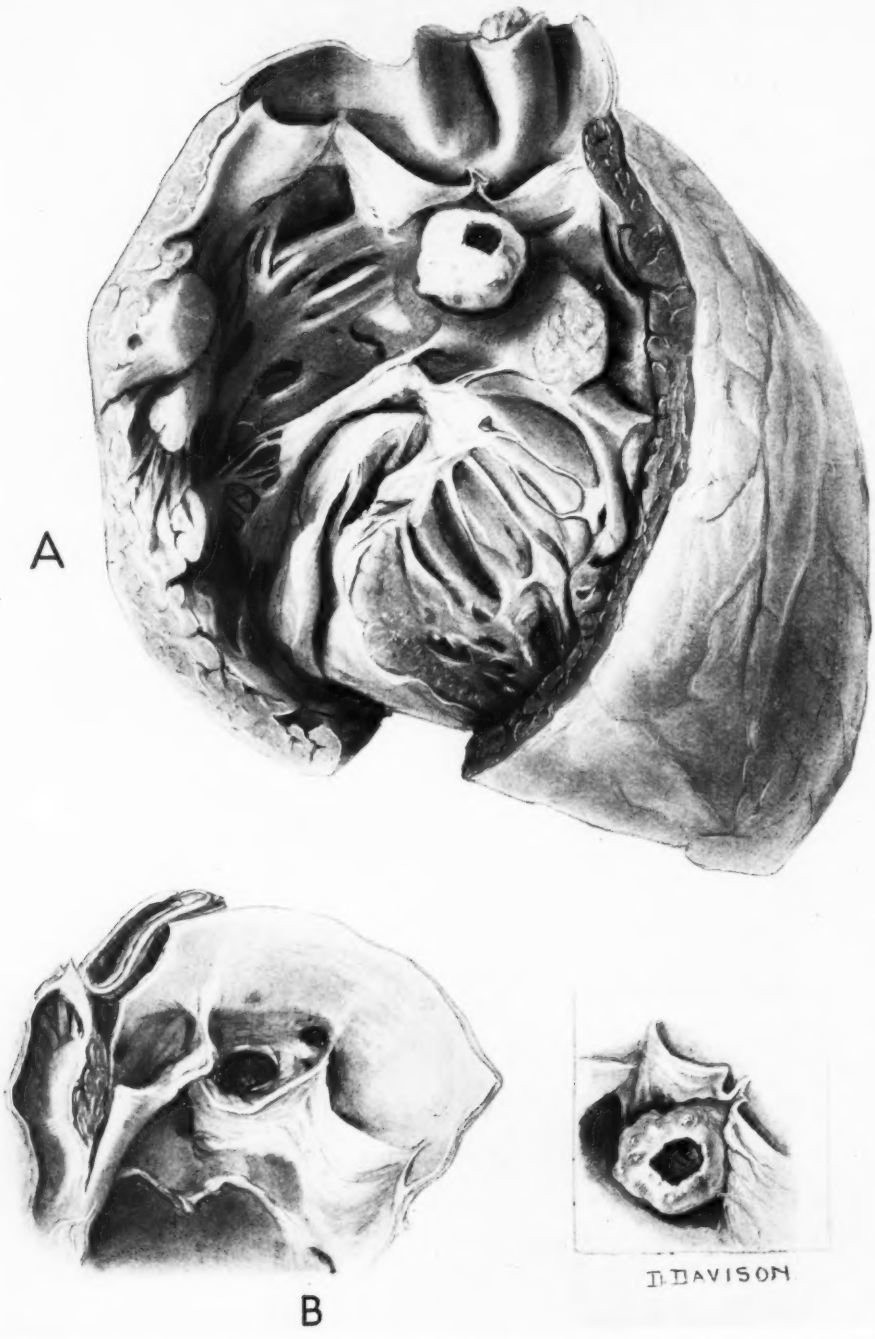

FIG. 4.—*Case* 2. *From a drawing of the heart.* (*A*) *Pulmonary and right ventricular aspect.* The perforated, globular aneurysm lies in the conus of the right ventricle just below the septal (posterior) and right anterior cusps of the pulmonary valve. (*B*) *Aortic and left ventricular aspect.* (*a*) The opening of the aneurysm in the right coronary sinus. The right coronary artery arises near the commissure between its sinus and the non-coronary sinus.

This abnormality occurred at about the level at which sub-aortic stenosis develops. The wall of the left ventricle was slightly thickened (1·5 cm.) and its cavity was dilated; this had led to the displacement of the ventricular septum towards the right ventricle. The wall of the right ventricle was about twice the normal thickness (0·9 cm.) and the columnæ carnæ and chordæ tendineæ were hypertrophied. The conus of the right ventricle was considerably dilated but its body appeared only slightly dilated, though this was difficult to estimate owing to the displacement of the ventricular septum. The circumference of the pulmonary valve measured 8 cm.; the septal cusp was fenestrated. The circumference of the aortic valve was 6·8 cm., and the left coronary cusp was slightly fenestrated. The mitral valve measured 7·5 cm. in circumference and the tricuspid valve 13 cm.; both valves appeared normal.

The absence of acquired heart disease and the presence of a congenital sub-aortic band of fibrous tissue make it reasonable to suppose that this aortic sinus aneurysm was of congenital origin. While unruptured it is unlikely to have given rise to symptoms, and it seems probable that the onset of symptoms 17 years before death coincided with rupture into the right ventricle; the healing of the margins of the rupture is consistent with this opinion.

Case 3. *A dissecting aneurysm of the right coronary sinus communicating with the right and left ventricles and leading to an intracardiac hæmatoma around the right coronary artery.*

In March, 1941, a married woman of 54 was admitted to hospital, complaining of vomiting and palpitation. Her previous health had been good except for an attack of rheumatic fever at age 27, when she was confined to bed for a year; she was subsequently told that she had a "weak heart." At 50, she noticed breathlessness on exertion and began to suffer from attacks of palpitation of sudden onset and offset, lasting 20 to 30 minutes. In June, 1940, she noticed increasing thirst, polyuria, and progressive weakness; a diagnosis of diabetes mellitus was made. She remained fairly well until two weeks before admission when she lost her appetite and became easily tired; for 48 hours before admission she vomited repeatedly and became drowsy. On the evening before admission she had an attack of palpitation which lasted several hours; during the night she awoke owing to a recurrence of the palpitation which continued until admission.

On *examination* it was found that the heart was completely irregular at a rate of 172 a minute. Blood pressure 120/85. The cervical veins were engorged and moist sounds were present at both lung bases. The temperature was 100° F. and the urine contained a considerable quantity of sugar and acetone; blood sugar 355 mg. per 100 ml. The condition was diagnosed as diabetes mellitus with hyperglycæmic pre-coma, and uncontrolled auricular fibrillation.

She was treated with insulin, glucose, and intravenous digoxin followed by digitalis by mouth. Her heart rate fell to 94 in 24 hours, when an apical diastolic murmur, typical of mitral stenosis, became audible. A cardiogram confirmed the presence of auricular fibrillation. A teleradiogram of the chest showed slight cardiac enlargement. The diabetic ketosis was rapidly controlled, but her temperature remained raised owing to a *B. coli* pyelitis which was treated by sulphapyridine. After three weeks she was allowed up for a short time; a week later she had an attack of paroxysmal nocturnal dyspnœa. She was confined to bed and the attacks ceased after four nights. Four days later she suddenly collapsed, complaining of tightness across the chest; she became cyanosed and died within a few minutes.

At *necropsy* effusions were present in both pleural cavities and there was generalized chronic venous congestion. The *heart* weighed 480 g.; the left ventricle was hypertrophied but the right appeared normal except where the aneurysm projected into it. Both atria appeared normal. The mitral valve was moderately stenosed; the aortic cusps were thickened but the pulmonary and tricuspid valves appeared healthy. There was slight atheroma of the coronary arteries, especially near the orifice of the right coronary.

The lower part of the right coronary sinus formed an aneurysm about 3 cm. deep extending towards, and projecting into, the conus of the right ventricle (Fig. 5). The upper part of the inner (aortic) wall of the aneurysm was formed by the right coronary cusp; the middle part of the wall was disorganized and interrupted by a perforation communicating with the left ventricle; the lowest part of the inner wall was formed by the upper part of the ventricular septum. The apex of the aneurysm projected into the right ventricle. The outer wall was formed by a large, grey, necrotic mass, 6 by 4 cm., which enclosed the first part of the right coronary artery. The upper part of this mass contained a recent hæmorrhage. The greater part of the aneurysm was lined by loose blood clot; when this was removed a smooth lining of adherent thrombus was seen.

Histology. Normally the annulus fibrosus is of triangular shape and covered by a thin layer of elastic tissue on its aortic and left ventricular surfaces (Fig. 6A); the aortic layer is continuous with

FIG. 5.—*Case* 3. *From a drawing of the heart.* (*a*) Aorta. (*b*) Aneurysm. (*c*) Hæmatoma.

the internal elastic tissue of the aorta and the ventricular layer joins the subendothelial elastic tissue on the left side of the ventricular septum and is continuous with the subendothelial elastic tissue of the right ventricle. In the specimen the annulus fibrosus had become separated from the aortic media. The left ventricular layer of elastic tissue of the annulus could be traced through to the elastic tissue on the left side of the membranous septum. At the apex of the aneurysm the distribution of elastic tissue strongly suggests that this was the reflected right side of the septum (Fig. 6C).

These observations are explicable if the aneurysm had been formed as suggested in Fig. 6. First, blood penetrated between the termination of the aortic media and the annulus fibrosus (Fig. 6B); then it spread into the subpericardial fat to form the large hæmatoma. It next separated the muscle of the right ventricle from the annulus and then extended in three directions, (1) to rupture through the endothelium of the right ventricle (2) to split the membranous septum and reflect it with its elastic layer towards the right ventricle, and (3) to sever the apex of the annulus from the septum and to rupture through the endothelium of the left ventricle (Fig. 6C). Thus the dissection lay between the annulus and the muscle of the right ventricle and had communicated with both ventricles.

Although there is little doubt that this was a dissecting aneurysm arising in the right coronary sinus at the junction of the aortic media with the annulus fibrosus, it is more difficult to decide the nature of the lesion that led to the dissection. Examination of the aorta showed none of the degenerative changes such as cystic medial necrosis often found in dissecting aneurysms. There were, however, inflammatory changes with a round-cell reaction, fibroblasts, and new capillaries. These changes were sometimes perivascular but, unlike the changes of syphilis, they were confined to the adventitia and did not invade the media. Although the inflammatory changes were most severe and acute at the point of rupture, they were also present in the whole of the intrapericardiac aorta. There were also striking histological changes in the aortic and mitral valve cusps, which were scarred and vascularized by thin-walled blood vessels, and in the myocardium small areas of perivascular fibrosis were found. In the pericardium there were recent inflammatory changes with some cellular foci which resembled Aschoff bodies, though giant cells were not found. The association of these changes in the valves and myocardium with mitral stenosis confirms their rheumatic origin and suggests that the recent inflammatory changes in the pericardium and aorta were due to a recrudescence of cardiovascular rheumatism. The close resemblance of the aortic lesions to those described as rheumatic aortitis by Pappenheimer and von Glahn (1924) strengthens this hypothesis. It is therefore probable that the dissection arose owing to the development of active aortitis, possibly rheumatic in origin.

Case 4. *An aneurysm of the non-coronary aortic sinus projecting into both atria, probably due to bacterial endocarditis.*

A married woman, aged 52, was first seen in June, 1942, on account of hæmatemesis due to a gastric ulcer. At this time a soft apical systolic murmur was noticed, but no signs of organic heart disease; blood pressure 135/85. Hæmatemesis recurred in

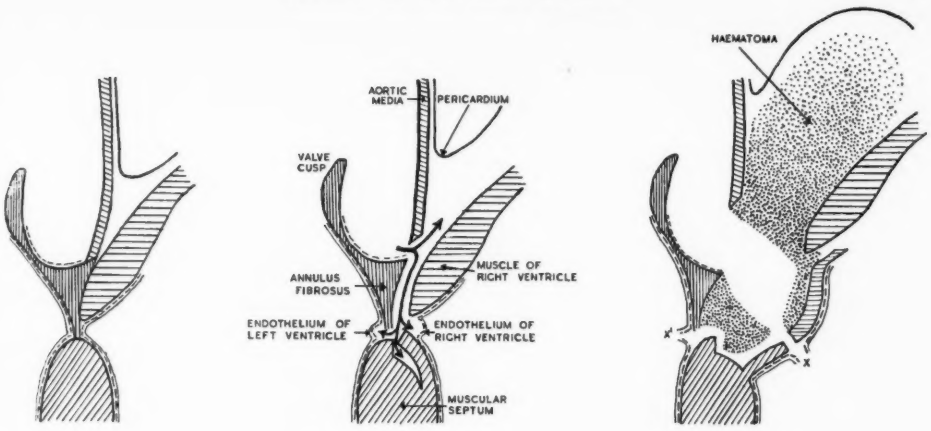

FIG. 6.—*Case* 3. *The formation of the aneurysm.* (*A*) *Normal structure of aortic root in section through right coronary sinus.* The distribution of elastic tissue is shown by interrupted lines. The structures are named in (*B*). (*B*) *Mode of dissection.* The annulus fibrosus has been separated from the termination of the aortic media; the subsequent directions of dissection are indicated by arrows. (*C*) *Aneurysm.* By comparison with (*B*) the way in which the aneurysm has formed can be seen.

June, 1943, and again in September, 1945, when she was re-admitted to hospital.

Examination. Blood pressure 140/90 mm. Apical systolic murmur still present. Hæmoglobin 74, falling to 64 per cent in a few days. Radioscopy showed the heart at the upper normal limit of size. Slight fever was present and persisted. White cell count 5800–7200 per c.mm. Gallstones were demonstrated by cholecystogram. Eleven septic teeth were extracted without any improvement in her condition. On January 4, 1946, she had a sudden gripping mid-sternal pain lasting twelve hours and became breathless. A systolic thrill and murmur then appeared in the 2nd left interspace near the sternum, and a high-pitched diastolic murmur along the left sternal border. The pulse became collapsing; blood pressure 145/55 mm. A diagnosis of ruptured aortic cusp due to infective endocarditis was made, and blood culture showed a non-hæmolytic, penicillin-sensitive streptococcus. In spite of apparent control of the infection with penicillin, she died from heart failure three weeks later.

At *necropsy* bilateral pleural effusion, general passive congestion, splenic and renal infarcts, and chronic gastritis were found. The *heart* weighed 470 g. From the non-coronary sinus an aneurysm, 2·5 cm. in diameter, projected backwards into the atria (Fig. 7 and 8). The interatrial septum ran across the aneurysm dividing it into two unequal parts, one-third lying in the right atrium and two-thirds in the left. The non-coronary cusp was thickened and calcified and, in the portion lying above the mitral valve, there was a perforation 1·7 cm. in diameter, surrounded by small crumbling vegetations. The other two aortic cusps were thickened and the commissure between them was calcified. Many small vegetations were present on the margins of all cusps. No abnormality was found in any other valve. The cavity of the left ventricle was moderately dilated and the ventricular wall slightly thickened. The other chambers appeared normal. Atheromatous changes were present in the coronary arteries but were not severe.

Histology. The wall of the aneurysm consisted of three layers; an outer layer of fibro-elastic tissue (the atrial endocardium), a middle layer of muscle, and a thick inner layer of fibrous tissue. The inner and middle layers were separated by small islands of elastic tissue which could be traced from the wall of the aneurysm into the elastic layer of the aortic media. Embedded in the inner layer were small areas of calcification. The aneurysm was partly lined by organizing thrombus which was sometimes covered by a thin layer of fibrous tissue. In the aortic adventitia adjacent to the aneurysm, there was a widespread, mainly polymorphonuclear, inflammatory reaction which had, at one point, spread into the aneurysm wall. Newly formed fibrous tissue extended from this area to the inner wall of the aneurysm and into the vegetations on the

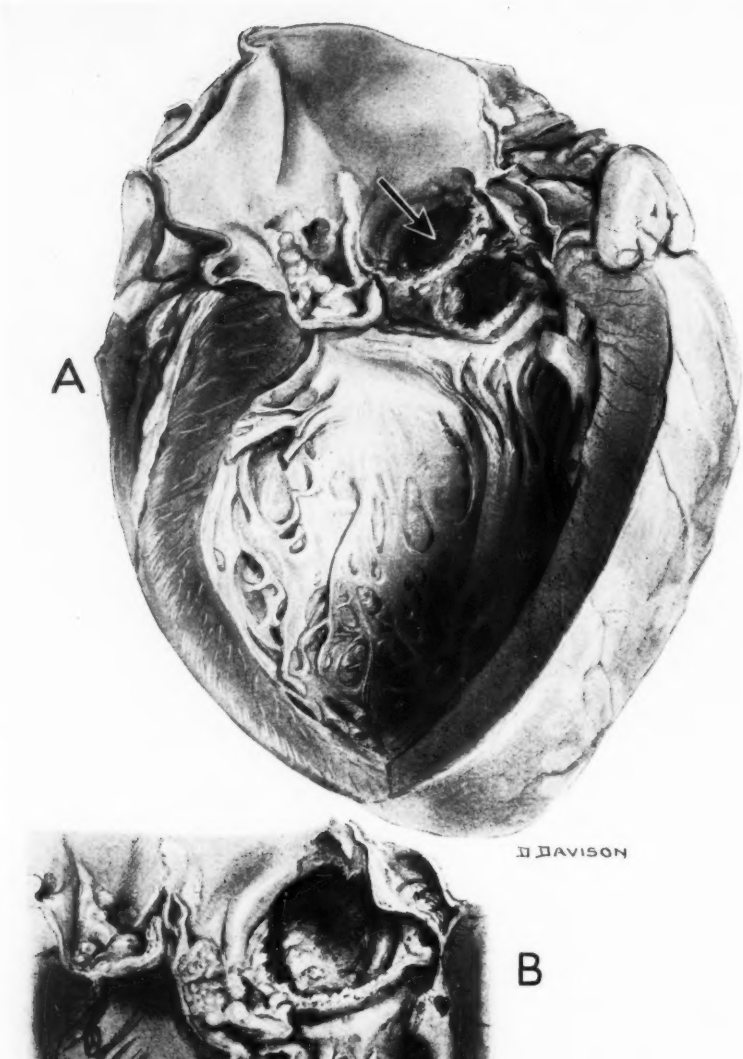

FIG. 7.—*Case* 4. *From a drawing of the heart.* (*A*) *Aortic and left ventricular aspect.* The arrow indicates the aneurysm; across its mouth a strip of tissue represents the remains of the non-coronary aortic cusp, below this lies the large perforation of the cusp. (*B*) The remaining part of the anterior aortic cusp has been removed to reveal the extent of the aneurysm. The vegetations of bacterial endocarditis are visible in (*A*) and (*B*).

FIG. 8.—*Case* 4. *From a drawing of the atrial aspect of the aneurysm.* The atrial septum, which crosses the aneurysm, has been cut. The left atrium and the mitral valve (M) lie to the left of the cut edge; the right atrium and the tricuspid valve (T) to the right.

non-coronary cusp. The aortic media was entirely free from inflammatory changes. The normal architecture of the non-coronary cusp was greatly distorted and much calcification was present. The histology of the mitral valve was normal. Sections from the ventricular septum showed a diffuse, fairly acute, myocarditis.

The aneurysm might have developed owing to the bacterial endocarditis, or it could have been of congenital origin and the focus for the bacterial endocarditis. It is not difficult to understand how the bacterial endocarditis could have led to this aneurysm for the position of the inflammatory reaction in the aorta was such that it might have caused a separation of the annulus fibrosus from the aortic media, thus exposing the muscle of the atria, which would be stretched by the intra-aortic pressure to form the aneurysm. In another case of subacute bacterial endocarditis we have seen the first stage of this process, for the annulus fibrosus of the non-coronary aortic cusp had been separated from the aortic media by a gap of 2 mm.; through this gap blood had penetrated to form a hæmatoma between the annulus fibrosus and the atrial muscle. If this had occurred in the present case and the separation had extended to expose the atrial muscle, thrombosus would have occurred on the exposed muscle surface and subsequent organization could have given rise to the fibrous lining of the aneurysm. The mode of formation thus resembles that in Case 3, but there the dissection started in the right coronary sinus and blood leaked into the loose subpericardiac tissues forming a hæmatoma. In the present case the leakage was limited by the close relationship of the non-coronary sinus to the atrial muscle, so a large hæmatoma could not form. We believe this to be the probable explanation of the histological structure of the aneurysm wall, so we do not suggest a congenital origin in this case. The absence of other congenital anomalies, which nearly always accompany congenital sinus aneurysms, supports this conclusion. There was no proof of an old lesion of the aortic valve upon which the bacterial endocarditis could have arisen, but the valve was so greatly deformed by the infection that old rheumatic disease cannot be excluded.

Cases 3 and 4 illustrate the difficulty that may be encountered in deciding the ætiology of sinus aneurysms, and emphasize the importance of adequate histological examination in these cases.

DISCUSSION

Aneurysms of the aortic sinuses may be divided into two groups; acquired (so-called "spontan-

eous") aneurysms, which arise in a diseased aorta, and aneurysms due to developmental defects. Since there appear to be important pathological, radiological, and clinical differences between the two types, which have not usually been described separately, we have considered it worthwhile to compare verified cases from both groups including our own cases and have collected 25 reported cases of congenital sinus aneurysms proved at necropsy, together with 22 acquired aneurysms *confined* to the aortic sinuses and confirmed pathologically. We have not included acquired aneurysms reported prior to 1914 since these were often inadequately described and the ætiological importance of syphilis was not appreciated. The sources of these cases are given below.

Congenital Aneurysms

*R.C.S.** Thurnam (1840); Beck (1842); Rickards (1881); Charteris (1883); Livingston (1883); Cayla (1885); Kryzwicki (1889); White (1892); Kraus (1902); Hart (1905) 3 cases; Eppinger (1916); Abbott (1919); Jacobi and Heinrich (1933); Hirschboeck (1942); King (1942); Macleod (1944); Our cases 1 and 2.

*N.C.S.** Goehring (1920); Laederich and Pomeau-Delville (1928); Duras (1944); Kawasaki and Benenson (1946); Herson and Symons (1946).

Acquired Aneurysms

*R.C.S.** Smith (1914) Cases 1 and 2; Noack (1919); Scott (1924) Case 1; Sheldon (1926); Abbott (1932); Benson, Hunter, and Manlove (1933) Case 1; Snyder and Hunter (1934) Case 2; Schuster (1937); Hamilton-Paterson and Castleden (1942) Case 3; Our case 3.

*N.C.S.** Marty and Froncin (1924); Norris (1932); Higgins (1934); Wright (1937); Our case 4.

*L.C.S.** Scott (1924) Case 2; Abbott (1932); Benson, Hunter, and Manlove (1933) Case 2; Snyder and Hunter (1934) Case 1; Ostrum, Robinson, Nichols, and Widman (1938) Case 5; Chipps (1941).

Morbid Anatomy

The figures below refer to the number of cases in which the feature mentioned has been recorded; since the descriptions are often insufficient, the figures are necessarily incomplete.

Congenital Aneurysms (25)

Sinus involved: *R.C.S.* 20; *N.C.S.* 5; *L.C.S.* 0.

Origin from sinus: Sac with round or oval opening 0·5 to 1·5 cm. sinus not dilated, 12. Whole sinus dilated, no separate aneurysmal sac, 2. Both dilated sinus and aneurysmal sac, 2.

Position of opening in sinus: *R.C.S.* right half, 3; central, 2; left half, 4. *N.C.S.* Adjacent to R.C.S., 3; central, 2.

Size: None larger than 4 cm. diameter.

Shape: Globular, unless ruptured; then collapse, unless thickened, to form fistulous channel 1·5 to 2·5 cm. long.

Walls: Thin, often transparent, but occasionally thickened.

Cardio-aortic fistulæ: *R.C.S.* 17 led to fistulæ; 13 to conus of right ventricle, 2 to right atrium, 1 to left ventricle, 1 to pulmonary artery. Fistulæ due to rupture of aneurysm, 12; probably present from birth, 5. *N.C.S.* 4 ruptured into right atrium. No congenital aneurysm ruptured outside heart.

Encroachment on intracardiac structures: *R.C.S.* Pulmonary valve, 6; tricuspid valve, 5; ventricular septum, 2; right ventricle, 1; both ventricles, 1. *N.C.S.* Right atrium, 5; tricuspid valve, 3; conducting bundle, 1.

Aortic incompetence: *R.C.S.* 4.

Associated lesions: Congenital: 23. Anomalies of aortic cusps, 15 (bicuspid, 6; much enlarged cusp, 4; rudimentary cusp, 1; thickened cusp, 4; calcified cusp, 2; fenestrated cusp, 2). Subaortic stenosis, 2. Abnormal extension of annulus fibrosus, 2. Ventricular septal defects, 10 (bulbar, 3; probably bulbar, 6; ruptured ventricular septal aneurysm, 1). Coarctation of the aorta, 2. Pulmonary conus stenosis, 1. Single coronary artery, 1. Patent foramen ovale, 1.

Acquired: Subacute bacterial endocarditis, 6. Rheumatic heart disease, 1.

Cardiac enlargement: Myocardial hypertrophy, 20; enlargement both ventricles, 14; mainly left ventricle, 4; mainly right ventricle, 4.

Heart weight: Less than 300 g., 3; 350 to 450 g., 2; 500 to 650 g., 5.

Summary. Congenital sinus aneurysms have been confined to the right coronary sinus and the adjacent two-thirds of the non-coronary sinus. They are always small but, owing to their thin walls, commonly rupture to form cardio-aortic fistulæ (21 of 25) usually communicating between the right coronary sinus and the right ventricle, or between the non-coronary sinus and the right atrium. They remain entirely intracardiac and do not affect extracardiac structures nor rupture outside the heart, but frequently cause disturbance of intracardiac structures, especially the pulmonary

* R.C.S. Right coronary sinus. N.C.S. Non-coronary sinus. L.C.S. Left coronary sinus.

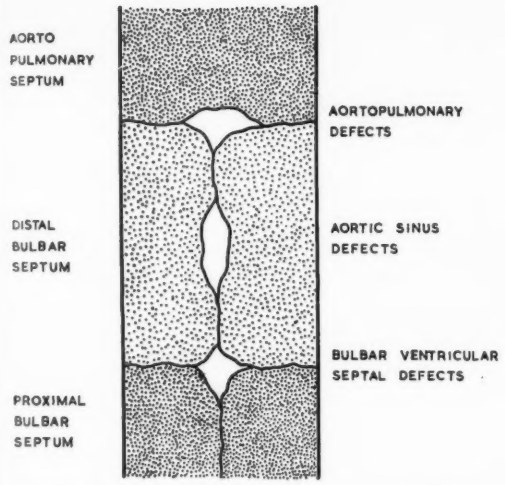

FIG. 9.—*Formation of the bulbar septum.* Fusion of the aortico-pulmonary and the proximal and distal bulbar septa occurs last at the areas represented as gaps. The suggested defects which may arise at these sites are indicated on the right.

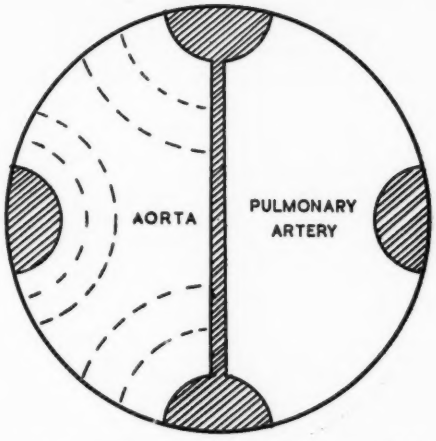

FIG. 10.—*Formation of the aortic cusps.* Growth of the cusps indicated by interrupted lines. Only two cusps can be related to the bulbar septum.

valve, which is often interfered with by right coronary sinus aneurysms, and the tricuspid valve which may be encroached upon by aneurysms arising in either sinus. Congenital sinus aneurysms are nearly always associated with other developmental faults, usually anomalies of the aortic cusps or bulbar ventricular septal defects. Apart from bacterial endocarditis, acquired heart disease has occurred in only one case.

Acquired Aneurysms (22)

Ætiology: Associated with syphilis, 17; with bacterial endocarditis, 4; dissecting, 1; atheromatous, 1.

Sinus involved: *R.C.S.* 11. *N.C.S.* 5. *L.C.S.* 7.

Size: Often very large, e.g. admitting two fists.

Rupture: *R.C.S.* 7 (right ventricle, 1; pulmonary artery, 2; pericardium, 1; left pleural cavity, 1; externally, 2). *N.C.S.* 3 (right atrium, 2; pericardium, 1). *L.C.S.* 1 (pulmonary artery).

Encroachment of intracardiac structures: *R.C.S.* Pulmonary artery, 1; right coronary artery, 4; tricuspid valve, 1; septum and conducting bundle, 1. *N.C.S.* 0. *L.C.S.* Pulmonary artery, 2; left atrium, 3; left coronary artery, 2; left ventricle, 1; mitral valve, 2.

Associated lesions: Aortic incompetence, 8 (syphilitic, 6; bacterial endocarditis, 2). Bicuspid aortic valve, 2.

Summary. Acquired sinus aneurysms may arise from any of the aortic sinuses. Owing to their large size they tend to extend upwards, often becoming extracardiac and rupturing outside the heart. Cardio-aortic fistulæ were present in only 6 cases. They encroach upon intracardiac structures less often than congenital aneurysms. Congenital cardiac defects were present in only two cases, but acquired heart disease was invariably present, usually syphilis or bacterial endocarditis.

EMBRYOLOGY

Congenital sinus aneurysms are believed to arise from defective development of the distal bulbar septum. This structure separates the systemic and pulmonary halves of the bulbus cordis, the primitive exit tube of the heart. It arises by endothelial outgrowths from each side of the bulbus cordis, and is completed by fusion distally with the aorto-pulmonary septum and proximally with the proximal bulbar septum, which represents the bulbar part of the ventricular septum (Fig. 9).

Congenital weaknesses are likely to develop at points of fusion, that is, distally, where the distal bulbar septum fuses with the aorto-pulmonary septum, between the two halves of the distal bulbar septum, and proximally where the distal meets the proximal bulbar septum (Fig. 10). It is reasonable to suppose that congenital aorto-pulmonary fistulæ

develop at the distal site, aortic sinus aneurysms and cardio-aortic fistulæ at the intermediate site, and bulbar septal defects at the proximal site of fusion.

Although all the aortic sinus aneurysms collected by Abbott (1919) arose from the right coronary sinus, aneurysms undoubtedly arising from the non-coronary sinus have been subsequently reported, but there is no reported instance of a congenital aneurysm arising from the left coronary sinus. From Fig. 10 it is clear that only two sinuses can be related to the distal bulbar septum, so it is not surprising that these aneurysms are confined to the right coronary and non-coronary sinuses.

Micks (1940) collected three cases of aneurysmal dilatation of all three aortic sinuses and added a new case; Brown (1939) also mentions a similar case. Micks tentatively suggested that such cases might be of developmental origin, but since neither syphilis nor cystic medical necrosis was excluded by adequate histological examination in any of these cases, we do not regard their developmental origin as proven.

Clinical Features of Congenital Sinus Aneurysms

Patients with congenital sinus aneurysms are usually male (19 of 24). Signs and symptoms might arise from (*a*) a cardio-aortic fistula, (*b*) interference with intracardiac structures, (*c*) other congenital defects, or (*d*) bacterial endocarditis.

Cardio-aortic fistulæ. A defect in the wall of an aortic sinus gives rise either to a congenital cardio-aortic fistula or to aneurysmal dilatation of the sinus that leads to a cardio-aortic fistula by rupture later in life; signs and symptoms due to the fistula may therefore either be present from birth or appear suddenly in later life.

Congenital cardio-aortic fistulæ. Five of the twenty-one fistulæ are believed to be congenital. In one case death occurred from pulmonary atelectasis ten days after birth and in another enterocolitis led to death at four months old; the aneurysms were incidental necropsy findings. In two other cases cardiac symptoms were minimal until two months and three years prior to death from heart failure at ages of 30 and 31; both patients had multiple congenital cardiac lesions including septal defects. The remaining patient never had cardiac symptoms, and death at age of 53 followed two weeks illness of unknown nature associated with severe vomiting and abdominal pain. Thus, death was due to intercurrent disease in three cases, and in the other two cases cardiac symptoms did not appear until the end of the third decade.

Cardio-aortic fistulæ due to sinus aneurysm rupture. Eppinger (1916) has described the event of rupture. A man of 43, previously fit and active, was climbing a mountain and bent down to lift a heavy stone; when about to cast this aside he was seized by a sudden pain in the chest and immediately noticed a "whirring" sensation in the mid-sternal area "like a half-filled bottle being shaken" in the chest. These sensations gradually diminished in severity and he was soon able to lead the way down the mountain. Eight days later he noticed difficulty in breathing and palpitation and soon became unable to walk more than a few steps; he was confined to bed and treated with digitalis without improvement; he developed œdema and died nine months later.

Of 25 congenital aneurysms, 15 are believed to have ruptured during life; in 6 cases death followed within five weeks and 6 died between two and thirteen months. Of the remaining 3 cases, one died four years after rupture due to further tearing of the aneurysm, a second died nine years later from bacterial endocarditis, and the third (our Case 2) survived seventeen years with intermittent failure, eventually dying with lobar pneumonia.

It therefore appears that the heart tolerates a congenital cardio-aortic fistula much better than its sudden development in later life, which usually leads to progressive heart failure, death occurring within a few weeks in over one-third of cases and within about a year in four-fifths of cases; in exceptional cases symptomatic recovery takes place, death being due to a second rupture or to intercurrent disease.

The physical signs of a cardio-aortic fistula are an important feature of congenital sinus aneurysms; for in only 4 of 25 cases was the aneurysm wall intact at death; in 13 cases the fistula led to the right ventricle, in 6 cases to the right atrium, in 1 case to the left ventricle, and there was an aorto-pulmonary fistula in the remaining case.

Both patency of the ductus arteriosus and aorto-pulmonary communications (Shepheard, Park, and Kitchell, 1944) give rise to a systolic-diastolic murmur at the base of the heart; and a collapsing pulse. But a communication between the greater and lesser circulations lying below the valve cusps, as in ventricular septal defect, causes only a systolic murmur. In cardio-aortic fistulæ one end of the fistula lies above the cusps, and one below, but there is no doubt that the associated murmur usually extends into diastole. This was so when there was no other congenital lesion (our Case 2) or only congenital lesions associated with systolic murmurs (10 cases). The character of this systolic-diastolic murmur is striking, for it is often described as superficial, simulating pericardial friction, and

nearly always coarse, harsh or rasping in character, accompanied by a thrill, usually systolic, but in Abbott's (1919) case there was a diastolic thrill so intense that it could be felt through the bedclothes. The systolic and diastolic components may merge into each other to form a continuous murmur so that the cardio-aortic fistula murmur is more likely to be confused with the murmurs of patency of the ductus or of a congenital aorto-pulmonary communication than with the to-and-fro murmurs of acquired aortic valve disease. The cardio-aortic fistula murmur tends to be lower in position than other continuous systolic-diastolic murmurs, and it was definitely louder in the third or fourth spaces than in either the second space in 6 of 9 cases in which this is recorded. The physical signs are essentially similar whether the fistula leads to the right ventricle or the right atrium. In the case reported by Herson and Symons (1946) the physical signs are of exceptional interest for, at the age of 12, before rupture, there was only a loud musical systolic murmur, maximal at the inner ends of the fourth and fifth interspaces, presumably due to the associated ventricular septal defect; whereas after rupture at the age of 31 the typical systolic-diastolic murmur became audible.

(*b*) *Interference with intracardiac structures:* The *aortic valve* was often affected and was incompetent in 7 cases, probably due to distortion by the aneurysm in 4 cases. There do not appear to have been striking symptoms until the aneurysm ruptured or bacterial endocarditis developed. The *tricuspid valve* was involved in 8 cases. In only 2 was a clinical diagnosis of tricuspid disease made; in these cases a systolic murmur was heard at the lower end of the sternum and hepatic pulsation was present. In 2 others, the necropsy findings suggested significant interference with the tricuspid valve, but in all 4 the patients had apparently been well and active until their aneurysms ruptured thirteen months, one month, four and a half weeks, and ten days before death. The *pulmonary* valve cusps were pushed aside in 5 cases; in none of these was pulmonary valve disease suspected during life, although pulmonary incompetence was diagnosed in another case in which the valve was not affected.

Pressure on the conducting bundle was believed to have led to the complete heart block in one case and pressure on the A-V node was regarded as the cause of A-V nodal rhythm in the other case. Encroachment upon the cardiac chambers has often occurred, but there is no evidence that it has impaired cardiac efficiency.

(*c*) *Associated congenital cardiac defects.* If a cardio-aortic fistula is present, its signs and symptoms overshadow those of other less striking congenital lesions, which can be studied only in cases with unruptured aneurysms and by reviewing the history prior to rupture in other cases. In two cases with unruptured aneurysms no clinical details are available, and in the other two there were no symptoms until bacterial endocarditis developed in the one case and Stokes-Adams attacks in the other. Of 15 patients whose aneurysms ruptured there were no cardiac symptoms prior to rupture in 14, and in the remaining one the incapacity was due to bacterial endocarditis. Ventricular septal defects were present in 6 cases, aortic incompetence in 3 cases, and slight coarctation of the aorta in 2 cases. The congenital defects associated with aortic sinus aneurysms appear to be of an almost asymptomatic type.

(*d*) *Subacute bacterial endocarditis.* Of 6 unruptured aneurysms, 4 became infected; 2 of these subsequently ruptured. Of 13 aneurysms that ruptured during life only one subsequently became infected, and that nine years later. The short duration of life after rupture may account for the rarity of subsequent infection. None of the five congenital communications became infected. Age does not appear to be a factor in determining the preponderance of infection in unruptured aneurysms, for the average age at death was similar in all groups and bacterial endocarditis developed at ages from one and a half to 56 years.

Causes of Death

Heart failure was the cause of death in 15 of 25 cases, and in 12 could be attributed to rupture, in 2 to congenital cardio-aortic fistulæ, and in 1 to rheumatic heart disease associated with an unruptured aneurysm. *Bacterial endocarditis* led to death in 6 cases, and *intercurrent disease* was the immediate cause of death in 4 cases. Thus, nearly two-thirds of these patients died from heart failure, usually due to the cardio-aortic fistula, and one quarter from subacute bacterial endocarditis.

In this summary of the clinical features of congenital sinus aneurysms the signs and symptoms associated with a cardio-aortic fistula have been emphasized, for this complication is present in the majority of cases, dominates the clinical picture by its often dramatic onset and striking physical signs, and usually leads to heart failure which is the commonest cause of death. By comparison, the effects of local extension of the aneurysm and the signs of other congenital defects are unimportant.

Radiography

Congenital sinus aneurysms are usually small and almost always project into a cardiac cavity rather than externally. It is therefore not surprising

to find that, in six published cases in which radiological findings are given, and in our two cases, no evidence of localized aneurysmal swelling was observed. Roesler (1943) and Ostrum *et al.* (1938) have described small projections from the vascular pedicle, often evident only in the oblique views, in cases of sinus aneurysm, but we conclude that these observations relate to the acquired variety. In eight cases with radiological findings, the heart was enlarged in all. In seven of them a cardio-aortic fistula was present and probably responsible for the enlargement; in the remaining case a ventricular septal defect and aortic incompetence were present. The available evidence indicates that the enlargement involves both ventricles. The aortic shadow was not abnormal in four cases where this point is recorded.

Electrocardiography

Only two electrocardiograms have been published, and the findings are described in three other cases. Including our two cases, we have information about the standard limb leads in only seven cases. In two cases right axis deviation was associated with signs suggestive of aortic incompetence, though actually due to the cardio-aortic fistula; some diagnostic significance was assigned to this association by Hirschboeck (1942) and Herson and Symons (1946) but it has not occurred in the other cases, left axis deviation being present in three cases. Complete heart block and auricular fibrillation have each occurred in one case. The electrocardiographic findings are so inconstant that they give little assistance in diagnosis.

Diagnosis of Congenital Sinus Aneurysms

An unruptured congenital aortic sinus aneurysm is almost asymptomatic and without physical or radiographic signs, though the presence of congenital heart disease may be recognized by the signs of an associated lesion such as a bulbar septal defect. Unruptured sinus aneurysms are, however, very prone to become infected, as we have shown, and when bacterial endocarditis develops in a heart apparently previously healthy, this is one of the silent underlying lesions that may be suspected.

The situation is quite different when a cardio-aortic fistula is present, either congenital or due to the rupture of a sinus aneurysm, for this is associated with striking physical signs and, if due to rupture in later life, with a dramatic clinical history. Eppinger (1916) was able to make a correct clinical diagnosis in his case by comparing the event of rupture during effort and the physical signs that followed with the similar case described by Kraus (1902). Rupture of a congenital sinus aneurysm is perhaps most likely to be confused with rupture of an aortic cusp, though this is usually associated with either syphilis or bacterial endocarditis. If these two diseases can be excluded rupture of a sinus aneurysm may justifiably be suspected, unless it is to be admitted that a healthy aortic cusp can rupture owing to exceptional trauma. In this differential diagnosis the physical signs will be helpful for the characteristic harsh, superficial, systolic-diastolic murmur, often accompanied by a thrill, maximal in the third left interspace near the sternum should differentiate a cardio-aortic fistula from aortic incompetence but the accompanying Corrigan pulse gives little help for it is present in both conditions.

It is more doubtful whether a precise diagnosis can be made when the cardio-aortic fistula is present from birth for the advantage of the characteristic history of rupture is lost. The nature of the murmurs and their presence from early life will suggest a congenital heart lesion but it will almost certainly be impossible to distinguish between an aorto-pulmonary fistula and a cardio-aortic fistula and the differential diagnosis from patency of the ductus arteriosus may be difficult. The more superficial and harsher murmurs, situated unusually low for that of a patent ductus, and the more striking Corrigan pulse, may lead to the suspicion of a cardio-aortic fistula, but these qualities are merely a matter of degree and it must be admitted that no reliable differential sign is available. Electrocardiography and radiography will give little help unless an enlarged pulmonary artery suggests patency of the ductus, for it has not occurred in aortic sinus aneurysms. Since surgical ligation of the ductus has become commonplace, it is fortunate that congenital cardio-aortic fistulæ are rare.

Summary

The nomenclature of the aortic sinuses is discussed and the topography of the aortic root illustrated.

Four cases with aortic sinus aneurysms, two congenital and two due to aortic disease, are described.

Including these cases, a verified series of 25 congenital and 22 acquired sinus aneurysms has been collected.

The pathological features of the condition are illustrated by an analysis of this series of cases.

The embryology of congenital sinus aneurysms is briefly discussed.

The clinical features of congenital sinus aneurysms are described and diagnosis is discussed. Attention is directed to the striking clinical features associated with a cardio-aortic fistula.

When a congenital sinus aneurysm ruptures in later life we may, from the combination of history and physical signs, expect to recognize the presence of cardio-aortic fistula; if a congenital cardio-aortic fistula is present the existence of a congenital heart lesion will be manifest and, from the physical signs we may suspect the presence of a congenital cardio-aortic fistula or an aorto-pulmonary communication. Finally, although we cannot hope to diagnose an unruptured aortic sinus aneurysm, it is, like a bicuspid aortic valve, one of the silent congenital lesions to be suspected when bacterial endocarditis develops in a heart apparently previously healthy.

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REFERENCES

Abbott, M. E. (1919). *Contr. med. biol. Res.* (Osler Memorial), **2**, 899.

—— (1932). *Libman's Ann.*, **1**, 23.

—— (1936). *Atlas of Congenital Heart Disease*, New York, p. 36.

Bauer, D. de F., and Astbury, E. C. (1944). *Amer. Heart J.*, **27**, 688.

Beck, T. S. (1842). *Med.-chir. Trans.*, **25**, 15.

Benson, R. L., Hunter, W. C., and Manlove, C. H. (1933). *Amer. J. Path.*, **9**, 295.

Brown, J. W. (1939). *Congenital Heart Disease*, London, p. 184.

Cayla, A. (1885). *Progr. med., Paris*, 2nd ser., **2**, 121.

Charteris, M. (1883). *Med. Pr.*, **35**, 354.

Chipps, H. D. (1941). *Arch. Path.*, **31**, 627.

Duras, P. F. (1944). *Brit. Heart J.*, **6**, 61.

Eppinger, H. (1916). *Wien. med. Wschr.*, **66**, 65.

Goehring, C. (1920). *J. med. Res.*, **42**, 49.

Hamilton-Paterson, J. L., and Castleden, L. I. M. (1942). *Brit. Heart J.*, **4**, 103.

Hart, K. (1905). *Virchow's Arch.*, **182**, 167.

Herson, R. N., and Symons, M. (1946). *Brit. Heart J.*, **8**, 125.

Higgins, A. R. (1934). *Nav. med. Bull., Wash.*, **32**, 47.

Hirschboeck, F. J. (1942). *Amer. Heart J.*, **24**, 550.

Jacobi, M., and Heinrich, A. (1933). *Amer. J. med. Sci.*, **186**, 364.

Kawasaki, J. A., and Benenson, A. S. (1946). *Ann. intern. Med.*, **25**, 150.

King, J. T. (1942). *Principles and Practice of Cardiology* (Bramwell & King), Oxford, p. 311.

Kraus, Fr. (1902). *Berl. klin. Wschr.*, **39**, 1161.

Krzywicki, C. (1889). *Beitr. path. Anat.*, **6**, 463.

Laederich, L., and Poumeau-Delville, G. (1928). *Bull. Soc. med. Hop. Paris*, **35**, 1734.

Livingston, B. (1883). *Med. Rec.*, New York, **24**, 249.

Macleod, A. (1944). *Brit. Heart J.*, **6**, 194.

Marty, P., and Froncin, J. (1924). *Bull. Soc. Anat. Paris*, **94**, 580.

Micks, R. H. (1940). *Brit. Heart J.*, **2**, 63.

Noack, F. K. (1919). *Zbl. Herz-u. Gefasskr.*, **11**, 233; 245.

Norris, J. C. (1932). *Nav. med. Bull., Wash.*, **30**, 37.

Ostrum, H. W., Robinson, B. D., Nichols, C. F., and Widman, B. P. (1938). *Amer. J. Roentgenol.*, **40**, 828.

Pappenheimer, A. M., and von Glahn, W. C. (1924). *J. med. Res.*, **44**, 489.

Roesler, H. (1943). *Clinical Roentgenology of the Cardiovascular System*, Baltimore, pp. 327, 407.

Rickards, E. (1881). *Brit. med. J.*, **2**, 71.

Schuster, N. H. (1937). *Lancet*, **1**, 507.

Scott, R. W. (1924). *J. Amer. med. Assoc.*, **82**, 1417.

Sheldon, J. H. (1926). *Lancet*, **1**, 178.

Shepheard, S. G., Park, F. R., and Kitchell, J. R. (1944). *Amer. Heart J.*, **27**, 733.

Smith, W. A. (1914). *J. Amer. med. Assoc.*, **62**, 1878.

Snyder, G. A. C., and Hunter, W. C. (1934). *Amer. J. Path.*, **10**, 757.

Thurnam, J. (1840). *Med.-chir. Trans.*, **23**, 323.

Walmsley, T. (1929). *Quain's Elements of Anatomy*, Vol. 4, Part 3. London.

White, W. H. (1892). *Trans. path. Soc., Lond.*, **43**, 34.

Wright, R. B. (1937). *Arch. Path.*, **23**, 679.

THE Q–T INTERVAL IN ACUTE RHEUMATIC CARDITIS

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In the initial stages of rheumatic fever, carditis can usually be diagnosed with ease, since the significant murmurs are almost always to be heard. In the presence of polyarthritis, pyrexia, and raised sedimentation rate, it can be safely assumed that this carditis is active. It may, however, be extremely difficult to determine how long such activity persists: the temperature and pulse rate may be normal, the electrocardiogram may show no gross changes, and such laboratory tests as are performed may show no abnormality, and yet, in some of these cases, it seems probable that carditis is still active. This study is an attempt to use electrocardiographic data to supply criteria of such sub-clinical activity.

Donders (1868) originally studied the duration of systole on the radial plethysmograph. Two years later Garrod (1870), using the same technique, evolved a formula for correcting the first, or systolic portion of the plethysmograph, for heart rate, and suggested that alterations in the duration of systole might be useful in the diagnosis of heart disease.

Berliner in 1931 first noted that prolongation of the Q–T interval of the electrocardiogram occurred in rheumatic valvular disease. Drawe *et al.* (1937) measured the Q–T interval in 100 rheumatic and 100 normal children. They showed that 25 per cent of the former and 4 per cent of the latter were above the upper limit of normal as judged by Ashman and Hull's (1937) criteria. They did not state, however, whether acute carditis was present when this measurement was taken. Taran and Szilagyi (1947) found that the duration of electrical systole, both absolute and relative to diastole, was significantly lengthened in all cases of acute rheumatic carditis. They further stated that this prolongation was not a function of the cardiac rate, but rather of the severity of the disease; that this prolongation preceded all other laboratory criteria of rheumatic activity, and that it did not return to normal until long after all other diagnostic signs had reverted to normal.

In view of the importance of this statement an investigation was undertaken to see whether prolongation of the Q–T interval was a reliable index of active carditis and whether it could prove of prognostic significance.

Material

In all, 134 cases were studied. The patients were under treatment in the special unit for juvenile rheumatism at the Canadian Red Cross Memorial Hospital, Taplow; no special selection of cases was made. Some were local patients, admitted in the initial stages of the rheumatic attack, but the majority were transferred from other institutions, provincial and metropolitan, throughout Great Britain, where they had already been under treatment for varying periods of time. The majority of the patients were children (see Table I).

TABLE I

Age Distribution

0– 5 years	6 cases
6–10 years	56 cases
11–15 years	50 cases
16–20 years	13 cases
Over 20 years	9 cases

On admission to hospital the cases were divided clinically into one of three main groups, those presenting evidence of active carditis, those presenting evidence of inactive carditis, and those cases in which no clinical carditis was detectable. Carditis was diagnosed clinically by the presence of one or more of the following: a diastolic murmur, cardiac enlargement, the presence of a pericardial friction rub, tachycardia out of proportion to elevation of temperature, and grosser electrocardiographic changes such as prolongation of P–R interval. Activity was recognized by pyrexia, tachycardia, and raised sedimentation rate.

The group of cases of active carditis was further subdivided into those patients who showed a steady

uninterrupted recovery and those who showed evidence of prolonged rheumatic activity.

TABLE II

CLASSIFICATION ACCORDING TO DEGREE OF CARDITIS OR ABSENCE OF CARDITIS

1. *Carditis*		
(i) Active carditis		
(*a*) Uninterrupted recovery	..	55 cases
(*b*) Prolonged activity	.. ..	45 cases
		100 cases
(ii) Inactive carditis	.. .. ..	12 cases
2. *No carditis*	.. ..	22 cases
		134 cases

METHODS

All electrocardiograms were taken on an American Cambridge continuous film electrocardiograph. The time marker was accurately checked against an oscillator of known frequency. All recordings were taken with the patient semi-recumbent at an angle of thirty degrees to the horizontal, Lombard and Cope (1919) having shown that systole varied with posture, being longer in the standing position.

The absolute Q–T interval varies slightly from complex to complex, as does the cycle length, but Katz (1921) showed that, while cycle length and the length of systole may vary phasically, these variations are not synchronous nor of like degree. To obviate distortion of cycle length by sinus arrhythmia, which in some cases was marked, the heart rate was calculated by counting the complexes over the entire length of tracing taken, covering at least two-thirds of a minute and usually one minute. The average cycle length was then calculated from the heart rate.

The Q–T interval was measured from the beginning of the Q wave until the end of the T wave in the standard lead in which the T wave was highest. This was usually lead two. At least six complexes were measured with calipers under a magnifying lens and the average length of the Q–T interval was taken.

The absolute duration of Q–T depends upon the heart rate, and thus measurements must be corrected for heart rate before they can be compared. Numerous formulæ exist for this correction (Lombard and Cope, 1919; Fridericia, 1920; Ashman and Hull, 1937; Schlamowitz, 1946). All these formulæ have been criticized, but the square root formula devised by Bazett (1920) is generally agreed to be one of the most reliable, and, because of its simplicity, has been used in this study. Taran and Szilagyi (1947) used Bazett's formula but expressed it as $K=\frac{Q-T}{\sqrt{C}}$ [where C=cycle length]. They called K the corrected Q–T or Q–Tc for short. This method and nomenclature have been adopted here.

Various values for the upper limit of Q–Tc have been laid down by different workers, Bazett (1920), Hegglin and Holzman (1937), Ashman and Hull (1937), and Taran and Szilagyi (1947). For this study electrocardiograms were taken on a short series of normal subjects; the upper limit of normal for Q–Tc was found to conform to Ashman and Hull's criteria which, accordingly, were adopted. Therefore the upper limit of the normal for Q–Tc has been taken as 0·422 second for men and children and 0·432 second for women.

RESULTS

(1) *Q–Tc and heart rate.* It is imperative that any formula which is employed to correct Q–T for cycle length must not be distorted by extremes of heart rate. Bazett's formula was tested as shown in Fig. 1, in which 426 measurements of Q–Tc from

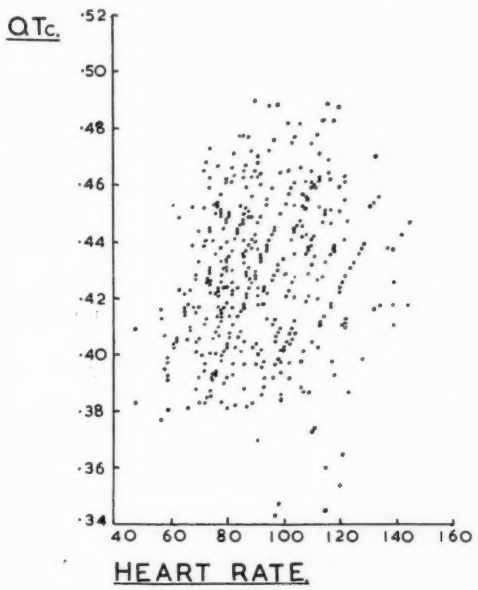

FIG. 1.—Q–Tc correlated with heart rate.

80 patients, both with and without carditis, are plotted against the heart rate.

The longest values for Q–Tc occurred with neither the slowest nor the most rapid heart rates, but did in fact appear at heart rates between 80 and 120. In the presence of active carditis it is natural that this degree of tachycardia should obtain.

TABLE III

RELATION OF QTc TO PRESENCE OF CARDITIS AND TO ITS DEGREE OF ACTIVITY

	Number of cases with carditis		Number of cases without carditis
	Active	Inactive	
Q–Tc prolonged	90	5	11
Q–Tc normal ..	10	7	11
Total ..	100	12	22

(2) *Q–Tc correlated with carditis.* Table III shows that the Q–Tc was prolonged in ninety of a hundred cases of active carditis. In the remaining ten cases the Q–Tc was within normal limits. Two of these patients had suffered previous pericarditis which was shown by Tung (1941) to shorten Q–Tc. In the remaining eight cases no factor was present that is known to shorten the Q–Tc. In this series the upper limit of normal was taken as 0·422 second for children as opposed to 0·405 second used by Taran and Szilagyi (1947). This may explain why only 90 per cent of these cases of active carditis showed a prolonged Q–Tc against 100 per cent in Taran and Szilagyi's series. Out of twelve cases with rheumatic heart disease, which were considered inactive on admission, five showed a prolonged Q–Tc. There was no other evidence of active carditis, but data given later in this paper tend to prove that this did exist. Of twenty-two cases considered to show no evidence of a heart lesion clinically, eleven cases showed a prolonged Q–Tc. Four of these cases were shown to have suffered carditis by the subsequent appearance of significant murmurs. It therefore seems probable that some of the remaining seven patients in this group suffered minimal cardiac damage, unrevealed by any of the criteria upon which a clinical diagnosis of carditis was made.

(3) *Q–Tc variation during the course of rheumatic fever.* The behaviour of Q–Tc was studied, both in patients making a rapid recovery from the rheumatic attack (Table II, Group (*a*)) and those showing prolonged rheumatic activity (Group (*b*)). The behaviour of Q–Tc in six cases belonging to Group (*a*) is shown in Fig. 2 and demonstrates the return of Q–Tc to normal with recovery.

Fig. 3 shows the behaviour of a typical Group (*a*)

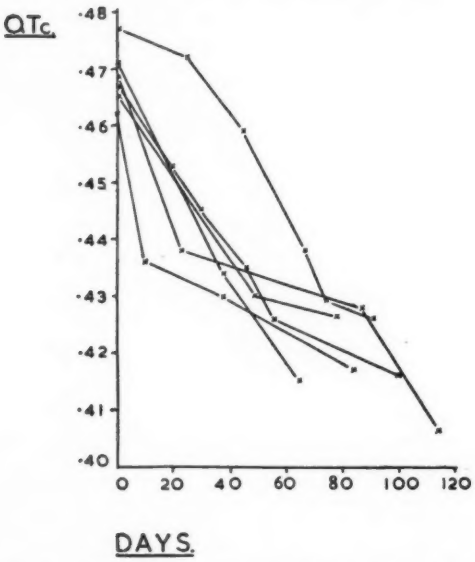

FIG. 2.—Behaviour of Q–Tc in six cases in Group 1 (*a*).

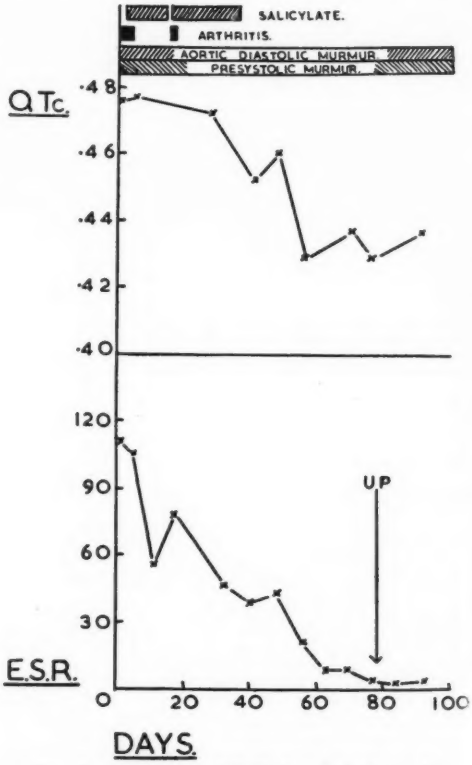

FIG. 3.—Behaviour of Q–Tc in a typical case in Group 1 (*a*).

case. This patient was admitted in the initial stages of her third attack of rheumatic fever. Mitral stenosis, due to previous rheumatic carditis, was present as witnessed by a presystolic murmur. On admission the sedimentation rate was raised and the Q–Tc was grossly prolonged, which was taken as evidence of acute carditis in this attack. With recovery her Q–Tc reverted to normal.

Fig. 4 and 5 demonstrate the behaviour of Q–Tc in two patients of Group (*b*) showing evidence of prolonged rheumatic activity, or what may be called chronic rheumatic carditis. Fig. 4 shows that although the sedimentation rate came down to normal occasionally, the Q–Tc was prolonged for the whole of the 240 days covered by the graph. Prolongation of Q–Tc may occur in chronic rheumatic heart disease without active carditis. This will be discussed later.

Fig. 5 illustrates another case in Group (*b*), in this instance complicated by congestive failure. Two points should be noted: the steady fall in sedimentation rate with the onset of congestive failure; and the rapid shortening of Q–Tc on two occasions when digitalis was exhibited. This effect was noted by Cheer and Dieuiade (1931). This latter point is also illustrated by Fig. 6 which shows the shortening of Q–Tc in two normal patients when digitalis was exhibited. In neither of these patients was the direction of the T wave seen to change in the electrocardiograms subsequent to the administration of digitalis.

Fig. 7 illustrates the effect on Q–Tc of an exacerbation of rheumatic carditis. When admitted, this patient was judged to be quiescent, following a second attack of rheumatic fever. The antistreptolysin titre was 150 units, the sedimentation rate was normal, and the Q–Tc was not prolonged. Established heart disease was present and rheumatic nodules were noted. He then developed scarlet fever; the Q–Tc immediately rose and at the same time the P–R interval lengthened from 0·16 to 0·27 sec. The antistreptolysin titre rose to 400 and later to 833 units. The sedimentation rate also rose and he suffered a severe exacerbation of carditis. The P–R interval first came back to normal; this was followed by a return to normal of the sedimentation rate. The Q–Tc, however, remained prolonged. In the present series the P–R interval was always found to be normal when the Q–Tc was within normal limits.

(4) *Correlation of Q–Tc and sedimentation rate.* The sedimentation rate still remains one of the most

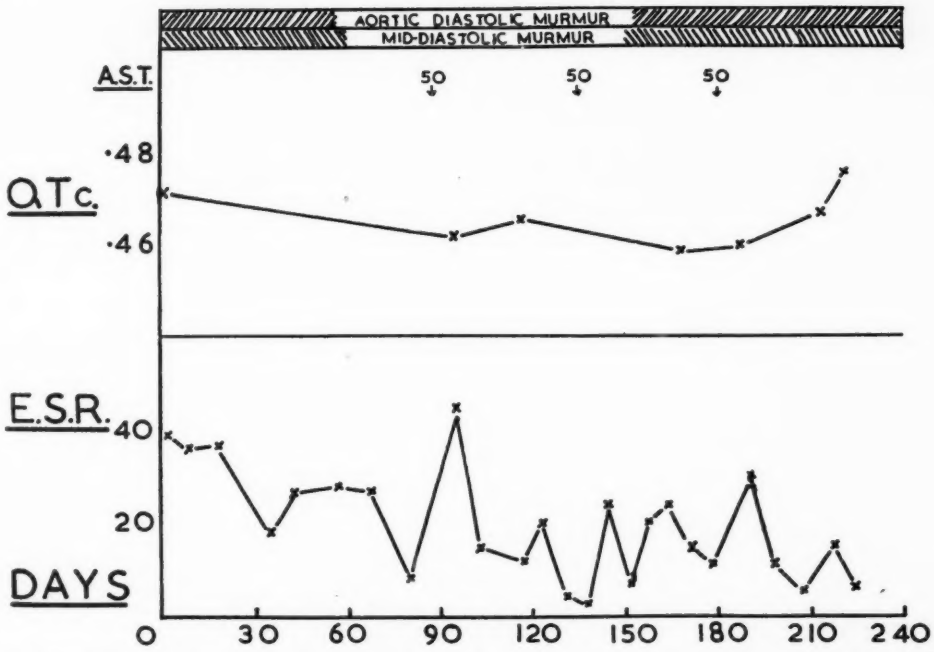

FIG. 4.—Behaviour of Q–Tc in chronic rheumatic carditis: Group 1 (*b*). A.S.T. = Antistreptolysin "O" titre.

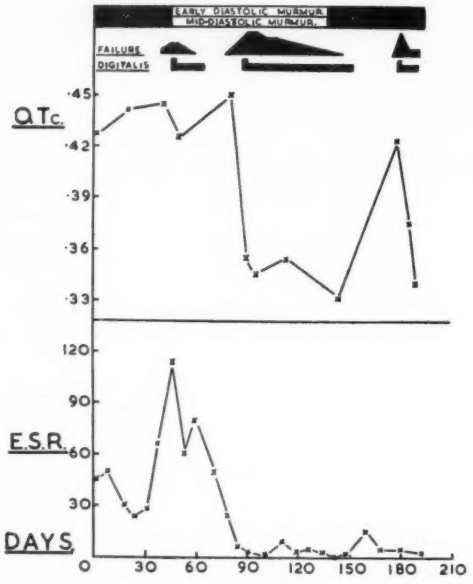

FIG. 5.—Behaviour of Q–Tc in another case with chronic rheumatic carditis. Note influence of digitalis on the length of Q–Tc, and the fall in ESR with the onset of congestive failure.

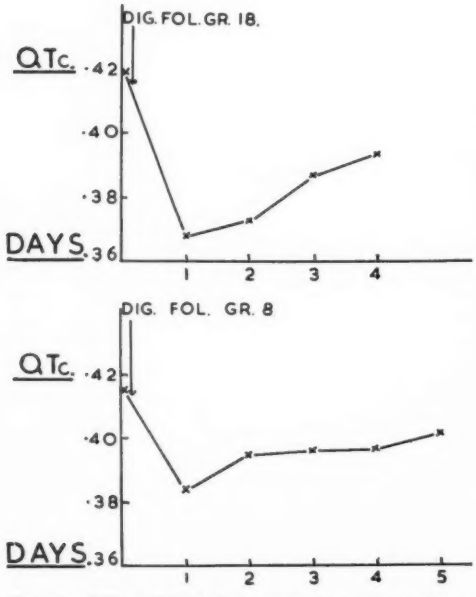

FIG. 6.—Effect of digitalis on Q–Tc in normal subjects.

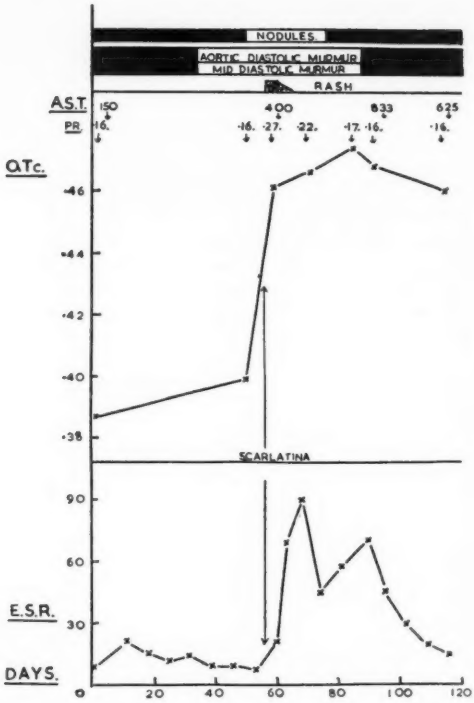

FIG. 7.—Recurrence of rheumatic carditis and Q–Tc. PR = P–R interval in seconds.

important signs of rheumatic activity; accordingly, the duration of Q–Tc was compared with the sedimentation rate in patients with, and without, carditis. The results are illustrated in Fig. 8.

In Fig. 8, 293 readings of Q–Tc from sixty patients with active carditis are plotted against the sedimentation rate on a semi-logarithmic scale, and it will be seen that, in general, the length of Q–Tc varies directly as the sedimentation rate. It will be noted, however, that some patients with active carditis show a short Q–Tc in spite of a high sedimentation rate; some of these patients were suffering from pericarditis, and others were receiving digitalis, the effect of this drug on systole being well known. It will also be observed that the Q–Tc was frequently prolonged when the sedimentation rate was within normal limits. Such observations were made towards the end of the patients' stay in hospital, and illustrate the persistence of a long Q–Tc at a time when other evidence of activity, such a the sedimentation rate, had subsided.

Fig. 9 shows 36 readings of 11 patients with

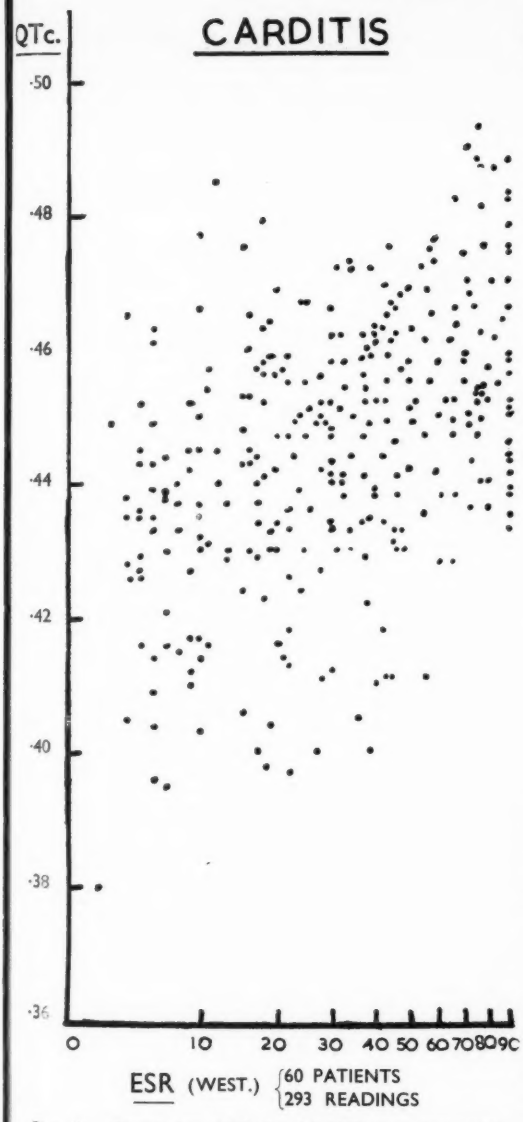

FIG. 8.—Correlation of Q–Tc with ESR in patients with active carditis. Compare Fig. 9.

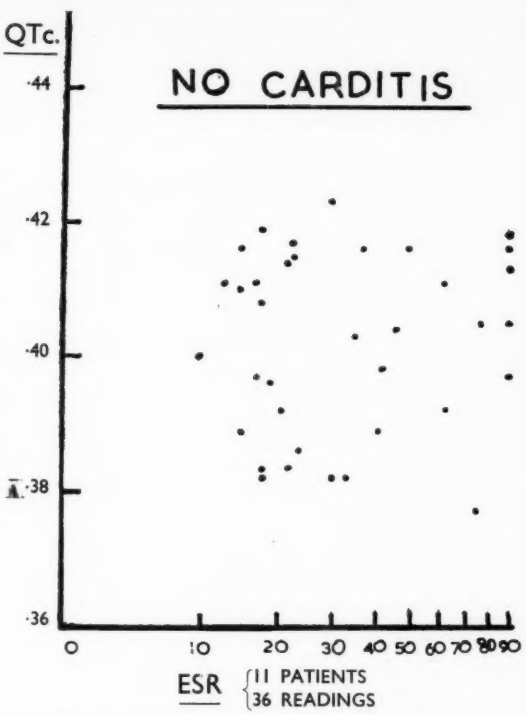

FIG. 9—Correlation of Q–Tc with ESR in patients with acute rheumatic fever without carditis.

acute rheumatic fever, but no clinical evidence of carditis; the Q–Tc is below the upper limit of normal in every case, and bears no relationship to sedimentation rate.

(5) *Q–Tc and relapses.* These findings confirm Taran's claim that prolongation of Q–Tc is a reliable index of active carditis. It follows therefore that increase in physical activity in the presence of a prolonged Q–Tc might theoretically be expected to precipitate a relapse. The relapses that occurred were analysed accordingly. Fig. 10 illustrates this point.

This child was admitted in the middle of a severe attack of rheumatic carditis. The Q–Tc was grossly prolonged, the sedimentation rate was raised, erythema marginatum was noted, and a crop of nodules appeared. After 90 days in hospital the Q–Tc and the sedimentation rate were within normal limits. At this point she suffered another β-hæmolytic streptococcal infection, which was followed by a severe exacerbation of carditis; the Q–Tc rose and a slower rise in sedimentation rate occurred. Rash and nodules re-appeared. Two hundred and sixty days after admission the sedimentation rate, temperature, and pulse rate had returned to normal. She was then considered clinically inactive and was allowed up, in spite of a prolonged Q–Tc. An immediate relapse followed, accompanied by a further rise in Q–Tc and sedimentation

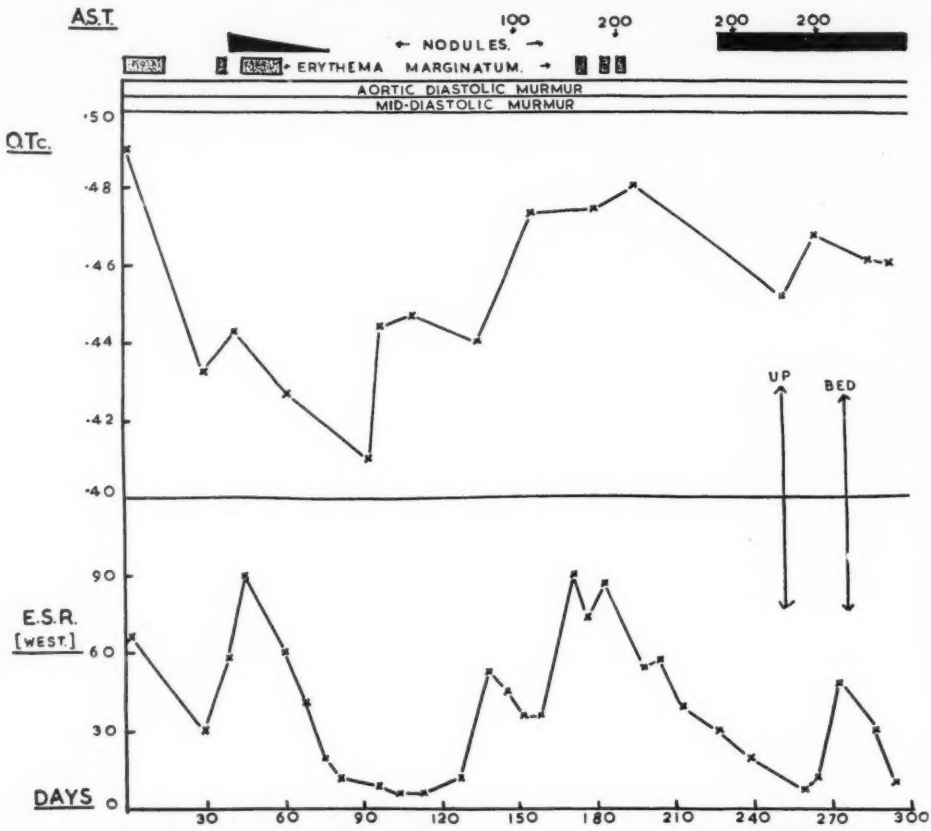

FIG. 10.—The effect of an increase in physical activity in the presence of a prolonged Q–TC.

rate, necessitating return to bed. The anti-streptolysin titre of 200 throughout this episode was very strong evidence against an occult streptococcal re-infection and subsequent rheumatic recurrence.

The criteria for judging an exacerbation of rheumatic carditis to be a relapse, rather than a recurrence, must be specified and adhered to rigidly. In much of the present series essential data were not obtained and definite conclusions could not be drawn. However, of twenty patients who apparently relapsed, fifteen were noted to have a long Q–Tc at the time that physical activity was increased. There was no other evidence of active carditis in any of these patients. This and other material is now under careful analysis to find out whether prolongation of Q–Tc at the time that physical activity is increased is a significant factor in causing relapses.

DISCUSSION

These results prove that prolongation of Q–Tc occurs in active rheumatic carditis, but throw no light on the mechanism of its production. It is extremely doubtful if alterations in the diastolic filling pressure, or in the diastolic volume of the cardiac chambers, can be responsible, as in the majority of cases the venous pressure is not raised clinically. Prolongation of systole due to biochemical causes may be similarly discounted. In the patients who make an uninterrupted recovery from an attack of rheumatic carditis, it would appear that this prolongation depends upon actual involvement of the myocardium by the rheumatic process.

In chronic cases where the heart suffers prolonged myocardial and valvular damage, other factors are involved. In this group, actual muscular hypertrophy of the heart, consequent on valvular

deformity, may be responsible in part for prolonging Q–Tc. Even minor degrees of ventricular hypertrophy may now be detected by modern electrocardiographic methods. Prolongation of Q–Tc due to this cause has been noted by Berliner (1931) and Drawe *et al.* (1937). Comparable lengthening occurs in hypertensive heart disease, in cardiac failure from any cause, and in some cases of congenital heart disease, in particular, pulmonary stenosis. In all these conditions hypertrophy of the heart may occur and it seems possible that this increase in the bulk of heart muscle may lead to prolongation of Q–Tc. In cases in which the rheumatic process runs a severe and protracted course, giving rise to detectable ventricular hypertrophy, it would be unwise to ascribe prolongation of Q–Tc entirely to active carditis, especially when other signs of rheumatic activity are absent.

First degree heart block was noted in a number of patients. The incidence of this complication was not greater than has been previously described. It was noted, however, that prolongation of the P–R interval never occurred when Q–Tc was within normal limits, although the reverse obtained very frequently.

Until more complete data are available it does not seem justifiable to enforce long periods of bed rest when a long Q–Tc is the only abnormal finding. Further work on this aspect of the problem may be of great help in assessing the degree of physical activity that may safely be permitted in the individual case.

Summary and Conclusions

Prolongation of Q–Tc is a valuable index of active carditis in rheumatic fever, and active carditis may be detected by the presence of a prolonged Q–Tc long after all other clinical and laboratory criteria of activity have gone.

Prolongation of Q–Tc may be the only evidence of cardiac involvement in acute rheumatic fever.

In chronic rheumatic carditis, prolongation of Q–Tc may be due to causes other than active carditis.

Measurement of Q–Tc may be of help in assessing the degree of physical activity that may be allowed in the individual case.

I wish to express my thanks to Dr. E. G. L. Bywaters, Director of the Special Unit, for helpful criticism in the preparation of this paper.

I am also extremely grateful to Dr. Paul Wood for his advice and encouragement at all times.

References

Ashman, R., and Hull, E. *Essentials of Electrocardiography*. New York. The Macmillan Company. 1st edition, 1937.

Bazett, H. C. (1920). *Heart*, **7**, 353.

Berliner, K. (1931). *Amer. Heart J.*, **7**, 189.

Cheer, S. N., and Dieuiade, F. R. (1931). *Chin. J. Physiol.*, **5**, 217.

Donders, F. C. (1868). *Dublin Quart. J. med. Science*, **45**, 225.

Drawe, C. E., Hafkesbring, E. M., and Ashman, R. (1937). *Amer. J. Dis. Child.*, **53**, 1470.

Fridericia, L. S. (1920). *Act. med. Scand.*, **53**, 469.

Garrod, A. (1870). *Proc. Roy. Soc.*, **18**, 353.

Hegglin, R., and Holzmann, M. (1937). *Klin. Wschr.*, **16**, 1146.

Katz, L. N. (1921). *J. Lab. Clin. Med.*, **6**, 291.

Lombard, W. P., and Cope, O. M. (1918). *Proc. Soc. Exper. Biol. Med., N.Y.*, **16**, 97.

Schlamowitz, I. (1946). *Amer. Heart J.*, **31**, 329.

Taran, L., and Szilagyi, N. (1947). *Ibid.*, **33**, 14.

Tung, C. L. (1941). *Ibid.*, **22**, 35.

A CLINICAL TRIAL OF RAUWOLFIA SERPENTINA IN ESSENTIAL HYPERTENSION

BY

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In a casual perusal of papers on hypertension, one comes across well over a hundred so-called hypotensive remedies alleged to possess the property of lowering the blood pressure. In 1930, Ayman could collect over two hundred reports on the successful treatment of hyperpiesia by various hypotensive remedies.

In view of the persistently high mortality from hypertension in spite of the large number of measures recommended in the treatment of this disease one is forced to admit the futility or helplessness of the situation. In Ayman's opinion, the "proper treatment is still unknown." Evans and Loughnan, after a critical analysis and trial of thirty-three different preparations in seventy cases of high blood pressure (essential hypertension), were forced to admit the uselessness of them all. In their opinion, simple sedative measures are often more effective than the much more expensive and fashionable products extensively displayed on the market.

There is unfortunately, a great tendency on the part of both the medical profession and the laiety, to hail or applaud any new drug or measure introduced into the market, often on the basis of a few stray experiences or clinical impressions. In consequence of this attitude, many of the present day clinicians have learnt not to accept any claim for a new remedy unless and until its therapeutic value has been firmly established by resort to carefully controlled clinical observations.

My selection of *R. Serpentina* for the present study has not been entirely fortuitous. I have been prompted into the present enquiry by several factors. In the short span of ten years that the dried root of *R. Serpentina* has been on the market in India, in tablet form, there has been a growing demand in this country for these tablets. Preparations of the serpentina root have gained such unprecedented popularity for hypertension cases in this country, that there is hardly a patient with high blood pressure who has not been subjected to its effects in one form or another. One manufacturing firm alone claims to have sold over 50 million tablets of the dried root. One of the aims of the present investigations has therefore been to determine if this enthusiastic reception of the drug is warranted. As early as 1940, I had made the following allusion to the subject of *R. Serpentina* treatment in cases of hypertension: "After a trial of this preparation one finds it useful in a percentage of cases of hypertension only; the indications and suitability of the case for the drug have not as yet been worked out." Since that time, I have had the opportunity of observing the effects of this drug in a very large number of cases. After an extensive trial of various hypotensive remedies in several thousand cases of hypertension, both in private and hospital practice during the last ten years, I have found *R. Serpentina* to be the most consistently successful member of the whole group of hypotensive remedies. In reply to a recent questionnaire issued by me to fifty physicians from all over India, forty-six voted for *R. Serpentina* as being the best "hypotensive" in their experience.

In view of this overwhelming body of support in favour of regarding *R. Serpentina* as the remedy of choice, I have considered it opportune to subject this preparation to a more critical analysis and to try and form an unbiased opinion of its value as a hypotensive agent. In the present investigation I have tried to steer clear of those fallacies involved in the interpretation of therapeutic results, to which particular attention has been drawn by Ayman, Kapernick, and others. There is an unfortunate tendency to claim success in the treatment of essential hypertension merely on the basis of symptomatic improvement. In the opinion of Ayman, the successful treatment of hyperpiesia, implies, of neces-

sity, a substantial reduction in the level of the blood pressure. In Kapernick's opinion, "although symptomatic response is relatively easily obtained, reduction of blood pressure is difficult." This has been the experience also of Evans and Loughnan, who found that although good symptomatic relief can be obtained in cases of hypertension with a large number of remedies, the much more desirable hypotensive effect is rarely noted. The factor of natural lability of the blood pressure, so common in hypertensives, is often lost sight of, in the interpretation of results; as a result, perfectly normal or natural fluctuations are mistaken or misconstrued for evidences of the therapeutic value of the drug under trial.

According to Evans and Loughnan, any remedy before it can be accepted as having established a claim as a hypotensive agent must satisfy certain standards of efficiency, viz. (1) it should be capable both of reducing a blood pressure that is high and of maintaining it at the lowered value; (2) it should be able to exhibit its hypotensive action consistently and in a high proportion of patients; and (3) it should be free of all toxic ill-effects.

An Introduction to Rauwolfia Serpentina

The use of vegetable extracts in the treatment of high blood pressure is not new. Both, watermelon seeds and the mistletoe plant have been tried in the past, without gaining general endorsement. In 1939, Graham had reported benefit in cases of hypertension from the use of the tincture of hawthorne (*Cratægus oxycantha*).

R. Serpentina (variously known in India as sarpagandha, chandrika, chotachand, chandra, dhanmarna, dhan-barua, patala-gandhi, and covanamilpori) or the Serpentina plant is a large climbing or twining herb or shrub, belonging to the natural order *Apocynaceæ*, and found in the Himalayas, in Assam, Pegu, Tennasserim, Java, the Deccan peninsula, and the Malaya peninsula.

The root of this plant has been popular, both in India and in the Malay peninsula, from ancient times, as an antidote to the stings and bites of insects and poisonous reptiles. It has been used also as a febrifuge, as a stimulant to uterine contractions, for insomnia, and most of all for insanity. More recently, its clinical application has been extended, with success, to cases of high blood pressure.

Early researches on *R. Serpentina* showed that it contained an alkaloid which was provisionally called pseudobrucine. On account of its popularity with practitioners of indigenous medicine, the chemical composition of the serpentina plant has been subjected to considerable scrutiny. Sen and Bose (1931) discovered two alkaloids in its root, the total alkaloid content being about 1 per cent of the dried root, there being also a lot of resin and starch. Siddiqui and Siddiqui (1931) found, besides phytosterol, oleic acid, and unsaturated alcohols, five alkaloids, which were classified by them into two groups, viz. (1) The ajmaline group of three white crystalline, weak bases, ajmaline, ajmalinine, ajmalicine; and (2) the serpentine group of two yellow crystalline stronger bases, serpentine and serpentinine.

On the basis of experiments on frogs, Siddiqui and Siddiqui showed that the ajmaline group acts as a general depressant to the heart, respiration, and central nervous system, whilst the serpentine group causes paralysis of respiration, depression of nerves, and stimulation of the heart. Sen and Bose studied the pharmacological effects of the *R. Serpentina* alkaloids on cats and other higher animals. They reported a small drop of blood pressure, a stimulation of the respiration, a depression of the heart muscle and a relaxation of plain muscle-tissue (e.g. of the uterus and intestines). Roy (1931) found that large doses induce sleep, cause dulling of sensations and diminution of reflexes. Fatal doses caused death from respiratory failure the heart continuing to beat for some time after. Chopra has been engaged in pharmacological researches on the *R. Serpentina* since 1932, but the results of his work are not as yet known. It is claimed by certain manufacturers that the root from a well-reared and scientifically cultivated serpentina plant yields about three times more of the active alkaloids than the root from the wild plant, which is thinner, more stunted and often marred by exposure to the sun, rain, and frost.

On the basis of experimental and clinical studies, the root of *R. Serpentina* is said to have the following pharmacological attributes. (1) By action on the vaso-motor centre, it leads to generalized vasodilatation, with a lowering of blood pressure. (2) By depressant action on the cerebral centres, it soothes the general nervous system. (3) It exerts a sedative action on the gastric mucosa and a stimulating action on the plain musculature of the intestinal tract. (4) It stimulates the bronchial musculature.

A vague reference to the use of a tincture or alcoholic extract of the root of *R. Serpentina*, in cases of high blood pressure, was made in 1942 by Paranjpe. He claimed improvement, without any statistical backing, in most cases of hypertension; the hypotensive action was said to be particularly gratifying in elderly subjects and in the case of the diastolic pressure; the tincture was said to be a

good cough-sedative and diuretic. In two cases reported by Paranjpe, there had been a permanent reduction of blood pressure for well over a year, on occasional doses of the tincture.

Method of Investigation

Selection of patients. The fifty patients for investigation were selected from amongst a large number of cases of essential hypertension, who reported regularly at the clinic for treatment and who showed their willingness to co-operate. The diagnosis of essential hypertension was accepted on the basis of a routine clinical examination and investigations including urine analysis, ophthalmoscopic examination, orthodiagraphy, electrocardiography, and (in some cases) renal function tests and teleradiography. Only patients with systolic pressure over 160 and diastolic over 95 mm. were admitted into this series. Cases of nephritic or renal hypertension, secondary hypertension, and malignant hypertension (diagnosed on the basis of clinical and ocular criteria) were rigidly excluded. Of the 50 patients selected for study, 30 were males and 20 females, ranging in age from 39 to 76 years, the average age for the series being 59 years.

Each patient was instructed to report for examination periodically, according to a rigid and prearranged plan. The routine adopted in each case was identical, viz. after an initial examination and check-up of the blood pressure (reading A), the patient was kept on a sedative capsule (containing 0·25 grains of prominal or phemitone) given three times daily for two weeks, the blood pressure being recorded again (reading B) and accepted as the actual " pre-treatment " level. This preparatory period of sedation exerts in my opinion a sort of stabilizing influence on the blood pressure of hypertensives, especially in those with hypersensitive nervous systems. Administration of *R. Serpentina* tablets (one serpina tablet three times a day after meals) was then started, this dose being kept up for four weeks. The only other preparations permitted, during *R. Serpentina* therapy, were laxatives, insulin injections (in diabetics), and occasionally tablets of aspirin for headaches. During serpina treatment, the blood pressure was checked and recorded once weekly (readings C, D, E, and F). In a few of my cases, the fall was so precipitate that further treatment had to be discontinued. After four weeks of serpina treatment, all medication was stopped for four weeks; during this interval or period of no treatment, the blood pressure was recorded twice, at fortnightly intervals (readings G and H). A second course of serpina tablets (in the same doses) was then started and continued for two weeks; at the end of this course, the blood pressure was recorded for the last time (reading J). The following nine sets of blood pressure readings were, therefore, recorded in each case: (A) at start of investigation, (B) after two weeks of sedative therapy, (C) after one week of serpina therapy, (D) after two weeks of therapy, (E) after three weeks of therapy, (F) after four weeks of therapy, (G) after a fortnight of no medication, (H) after four weeks of no medication, and (J) after two weeks of serpina treatment (second course).

The ritual observed at each check-up of the patient was properly standardized. At each attendance (arranged between the hours of 3 and 6 p.m.), the patient was made to rest in the waiting room for about half an hour. After a short history of symptoms and an enquiry for toxic reactions, the patient was subjected to a thorough clinical examination. The blood pressure was recorded in the recumbent posture with the aid of a new Baumanometer, in accordance with the suggestions of the joint British and American Committees for standardization. Of three consecutive readings at each sitting, only the third or last was accepted for recording purposes. All the observations reported here were made by me using the same instrument throughout.

In the present investigation, I have not concerned myself much with the improvement in individual symptoms, reported by patients, such a determination being liable to errors of interpretation. In any case, the symptomatic status of such a case bears little or no relationship to the level of the blood pressure.

In the presentation of results, all rises or falls of systolic blood pressure of less than 10 mm. and of the diastolic of less than 5 mm. have been classified as " insignificant," rises or falls of systolic pressure between 10 and 24 mm. and of the diastolic between 5 and 14 mm. as " moderate " and rises or falls of the systolic exceeding 25 mm. and of the diastolic exceeding 15 mm. have been classified as "marked."

Results of Investigation

After two weeks of sedative therapy. After two weeks 28 of 50 patients showed a drop of systolic pressure ranging from 2 to 12 mm., the average fall being 6 mm. In 17 of the cases there was a rise ranging from 2 to 14 mm., with an average of 4 mm. In the remaining 5 cases, there was no alteration at all. Taking all 50 cases into consideration, the average drop of systolic blood pressure after two weeks of sedation works out at under 2 mm.

In the case of the diastolic blood pressure, there was a fall in 30 cases ranging from 2 to 8 mm. with an average of 3 mm.; in 7 cases there wa

an actual rise ranging from 2 to 10 mm., with an average of 4 mm.

After One Week of R. Serpentina Therapy

The immediate response of the blood pressure to *R. Serpentina* therapy is shown in Table I.

TABLE I

Changes of Systolic and Diastolic Blood Pressure after One Week of R. Serpentina Therapy

Extent of alteration in blood pressure	Systolic blood pressure		Diastolic blood pressure	
	No. of cases	Per cent	No. of cases	Per cent
From +10 to +6 mm.	1	2	1	2
+5 to +1 mm.	8	17	8	17
No change—	2	4	4	8
−1 to −4 mm.	7	15	18	38
−5 to −9 mm.	11	23	12	25
−10 to −14 mm.	7	15	4	8
−15 to −19 mm.	2	4	1	2
−20 to −24 mm.	5	10	0	0
−25 to −29 mm.	2	4	0	0
−30 to −34 mm.	2	4	0	0
−35 to −40 mm.	1	2	0	0
From +10 to −40 mm.	48	100	48	100

Systolic blood pressure. Of the 48 cases studied (two of our patients having absented themselves), as many as 37 cases showed a drop of systolic pressure, ranging from 2 to 38 mm. with an average drop of 13 mm. In 2 cases it remained unaltered whilst in 9 there was actually a paradoxical rise, ranging from 2 to 6 mm. with an average rise of 3 mm.

A " moderate " fall (i.e. 10 to 24 mm.) was noted in 14 out of 48 cases and a " marked " fall (i.e. 25 mm. or over) in 5 cases. In other words, of my 48 cases, 19 cases (or 39·5 per cent) showed a response within a week of commencement of serpina treatment.

Diastolic blood pressure. Of the 48 cases, 35 showed a fall of diastolic pressure ranging from 2 to 18 mm., with an average of 6 mm.; in 4 cases the diastolic level remained unaffected whilst in 9 there was an actual rise ranging from 2 to 6 mm. with an average of 3 mm.

The diastolic fall was classified as being of " moderate " degree (i.e. 5 to 14 mm.) in 16 cases and as " marked " (i.e. 15 mm. or over) in 1 case. A good result (i.e. a diastolic drop of 5 mm. or more) was therefore obtained in 17 cases. (See Table I.)

In 35 of my 48 cases, there was a drop of both systolic and diastolic pressure, after one week of drug treatment; in 6 cases there was a paradoxical rise of both systolic and diastolic pressure whilst in the remaining 6 cases there was a rise of one with a fall of the other.

After Four Weeks of R. Serpentina Therapy

The delayed response of the blood pressure to drug therapy is given in Table II.

TABLE II

Changes of Systolic and Diastolic Blood Pressure after Four Weeks of R. Serpentina Therapy

Extent of alteration in blood pressure	Systolic blood pressure		Diastolic blood pressure	
	No. of cases	Per cent	No. of cases	Per cent
From +20 to +11 mm.	1	2	0	0
+10 to +1 mm.	6	13	6	13
No change—	0	0	3	7
−1 to −9 mm.	5	11	17	36
−10 to −19 mm.	14	30	18	38
−20 to −29 mm.	9	19	2	4
−30 to −39 mm.	10	21	1	2
−40 to −49 mm.	1	2	0	0
−50 to −60 mm.	1	2	0	0
From +20 to −60 mm.	47	100	47	100

Systolic blood pressure. Of the 47 cases studied (three failed to report for check-up), as many as 40 responded to serpina therapy by showing a drop of systolic pressure, ranging from 2 to 54 mm. with an average of 21 mm. A rise of 4 to 12 mm., with an average of 6 mm. was noted in the remaining 7. Taking all the cases into consideration, the average fall worked out at 19 mm., with a range of +12 to −54 mm.

The systolic fall was described as being " moderate " in 22 cases out of 47 and as " marked " in 13 cases. In other words, a good systolic response (i.e. 10 mm. or over) was noted in 35 of 47 cases, after four weeks of serpina therapy.

Diastolic blood pressure. In 38 out of the 47 cases there was a drop of diastolic pressure ranging from 4 to 34 mm., with an average of 11 mm.; in 3 cases, the diastolic level remained unaltered whilst in 6 cases there was an actual rise varying between 2 and 10 mm., the average being 5 mm. Taking all cases into consideration, the diastolic pressure showed an average drop of 10 mm., the range of variation being from +10 to −34 mm.

The diastolic fall, after four weeks of therapy, could be classified as "moderate" in 27 of the 47 cases and as "marked" in 7 cases. A good diastolic response (i.e. 5 mm. or over) was therefore obtained in as many as 34 out of 47 cases.

In as many as 29 of my 47 cases there was a "moderate" or "marked" fall of both systolic and diastolic pressures; in 6 cases such improvement was confined to systolic levels only, and in 2 to the diastolic levels only.

Types of blood pressure response, during R. Serpentina therapy. According to the rapidity and degree of fall of the systolic blood pressure during drug treatment, I have been able to recognize five main types of blood pressure curves. (1) A gradual fall continued throughout the course of treatment (21 of my 50 cases). (2) The plateau type, where the systolic level showed little or no alteration throughout treatment (12 cases). (3) A precipitate initial drop with a gradual decline subsequently (8 cases). (4) An initial plateau with subsequently, a gradual decline (5 cases). (5) A precipitate initial drop with subsequently a plateau (3 cases).

From the behaviour of the pressure (especially systolic), a graph can easily be constructed to determine the type of response to drug treatment, in any given case.

After Cessation of R. Serpentina Therapy

These studies were undertaken with a view to determine whether the hypotensive action of serpina is strictly limited to the period of its administration or whether it is continued for some time after.

After two weeks. The persistence of the hypotensive action of *R. Serpentina* was studied in the 41 cases in my series, who had responded to its administration by a fall of blood pressure; unfortunately, 5 of these having failed to report for their periodical check-up, our enquiry has had to be limited to a total of 36 cases. Two weeks after stoppage of serpina treatment, the results were as follows. In 22 of the 36 cases the low levels induced by serpina tablets were well maintained; in 8 cases they were partially maintained; in 3 cases they had returned to their levels of before treatment; in the remaining 3 cases there was a further fall.

After four weeks. Thirty-nine cases could be investigated from this point of view. The results were as follows. In 10 the low levels were well maintained; in 15 cases they were partially maintained; in 10 cases they had returned to the level before treatment; in 4 cases the pressure showed a further drop. The hypotensive action of *R. Serpentina* was, therefore, perceptible in 91 per cent of my cases for two weeks and in 74 per cent for four weeks after discontinuance of the drug.

After a Second Course of R. Serpentina

In order to test the drug for consistency of action, all the 50 cases of my series were subjected to a second course of serpina tablets after an interval of four weeks. The tablets were administered in the same doses, but for two weeks only. The results of this second course were most satisfactory, making allowance for the fact that as many as 36 per cent of the cases were still under the hypotensive influence of the first course of tablets. The average drop of systolic blood pressure after the first course had worked out at 17 mm., the maximum fall recorded in any case being 44 mm. In the case of the diastolic pressure, the corresponding values worked out at 7 mm. and 22 mm. respectively.

After two weeks of the second course, the average systolic fall worked out at 10 mm., the maximum drop in any case being 24 mm. The corresponding values for the diastolic pressure were 5 mm. and 12 mm. respectively.

The blood pressure behaviour after the second course of tablets was very similar to that after the first, in the great majority of the cases. However, in one case there was a drop of pressure during the first course but a rise during the second; the reverse happened in one case.

Toxic Effects and Reactions from R. Serpentina

After having used the dried root of *R. Serpentina* in several thousand cases of high blood pressure, both in hospital and private practice, I can vouch for the non-toxicity of the drug with confidence; I have, so far, not come across a single fatality from the administration of this preparation. Even when the administration has been continued without a break for as long as two to five years (as in some of my cases), and even in the presence of cardiac or renal complications, there have been no ill-effects of a serious disabling or permanent nature.

The following reactions were reported by some of my cases, during the present investigation.

Excessive drowsiness or "sleepiness"	6 cases
Feeling of depression or lassitude	4 cases
Diarrhœa	3 cases
Anorexia	2 cases
Nausea and vomiting	2 cases
Vertigo or giddiness	2 cases
Increase of polyuria and nocturia	2 cases
Abdominal griping pain	1 case

The commonest disturbance after *R. Serpentina* administration, in my experience, has been that of

excessive drowsiness or sleep; to some of the hypertensives suffering from insomnia, this may prove a blessing in disguise. Diarrhœa is usually of a mild order and responds readily to treatment. On the whole, *R. Serpentina* preparations are very well tolerated by patients and appear non-toxic in therapeutic doses. The only contra-indications, in my opinion, are severe or intractable diarrhœas or dysenteries and cases of hypertension of renal or malignant type, where this form of treatment proves of no avail.

At the present time, *R. Serpentina* preparations, as manufactured in India, have one serious drawback to their use; not being properly standardized or assayed, the hypotensive action of the drug is not strictly constant from batch to batch of the drug. For some time now, the physicians of this country have felt the need for a more satisfactory and standard preparation of this drug, the action of which can be predicted at all times.

Summary and Conclusions

The hypotensive action of *Rauwolfia Serpentina* (N.O. *Apocynacæ*) has been subjected to clinical trial in a series of fifty cases of essential benign hypertension. Tablets of the dried root of this plant were prescribed in optimum doses, the patients being subjected to periodical check-ups of the blood pressure, according to a pre-arranged plan.

Within a week of *R. Serpentina* therapy, 77 per cent of my cases showed a drop of systolic blood pressure ranging from 2 to 38 mm., with an average drop of 13 mm. A drop of 10 mm. or over was noted in 40 per cent of cases.

In the case of the diastolic blood pressure, 73 per cent of cases displayed a drop ranging from 2 to 18 mm., with an average drop of 6 mm.; a diastolic response of 5 mm. or over was noted in 35 per cent. In 73 per cent of cases, there was a drop of both systolic and diastolic blood pressure after one week of therapy.

After four weeks of *R. Serpentina* therapy, 85 per cent of cases displayed a drop of systolic blood pressure varying from 2 to 54 mm. with an average of 21 mm. A systolic drop of 10 mm. or over was noted in as many as 74 per cent of cases.

In 81 per cent of cases, the diastolic pressure showed a drop of 4 to 34 mm. with an average of 11 mm. A diastolic fall of 5 mm. or over was noted in 72 per cent.

In 62 per cent of cases there was a " moderate " or " marked " drop of both systolic and diastolic pressure levels.

According to the behaviour of the blood pressure, I was able to recognize five types of response to *R. Serpentina* therapy, which have been described.

The hypotensive action was apparent in 91 per cent of cases two weeks after stoppage of all treatment and in 74 per cent even after four weeks of no treatment.

A second course, of two weeks, was tried in all the cases after an interval of four weeks; the blood pressure response to the second course of tablets was almost as good as during the first.

R. Serpentina appears to be a perfectly safe remedy, devoid of any serious or toxic ill-effects. Amongst the few unpleasant symptoms encountered during its administration, were excessive drowsiness (in 12 per cent), lassitude (in 8 per cent), diarrhœa (in 6 per cent), anorexia (in 4 per cent) and nausea with vomiting (in 4 per cent).

On the whole, the results of *R. Serpentina* therapy, in the present series, have been most encouraging. In most cases it was proved capable of lowering both systolic and diastolic blood pressure. Although its action is temporary in many cases, it can be reproduced successfully by a second administration of the drug. No serious reactions to therapy were encountered in any of the cases. *R. Serpentina*, therefore, satisfies all the criteria of a successful hypotensive agent formulated by Evans and Loughnan (1939). Judging from the results of the present investigation, it has a definite place in the treatment of cases of high blood pressure.

References

Ayman, D. (1931). *J. Amer. med. Ass.*, **96**, 1852.
—— (1932). *Ibid.*, **98**, 545.
Bhatia, B. B. (1942). *Jour. Ind. med. Ass.*, **2**, 262.
Chopra, — (1933). *Indigenous Drugs of India*, Calcutta.
Evans, W., and Loughnan, O. (1939). *Brit. Heart J.*, **1**, 199.
Kapernick, J. S. (1943). *Amer. Heart J.*, **26**, 610.
Paranjpe, A. S. (1942). *Med. Bull.*, **10**, 135.
Roy, P. C. (1931). *Patna J. Med.*, **4**, 131.
Sen, G., and Bose, K. (1931). *Ind. med. World*, **2**, 194.
Siddiqui, S., and Siddiqui, R. H. (1931). *Jour. Ind. Chem. Soc.*, **8**, 667.
Vakil, R. J. (1940). *Med. Bull.*, **8**, 15.
—— (1942). *Ibid.*, **10**, 177.

THE PHONOCARDIOGRAPHY OF HEART MURMURS

PART I.—APPARATUS AND TECHNIQUE

BY

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It was considered important to subject the points made by William Evans (1947) to further examination by phonocardiography. We hoped to define the sphere of usefulness of this instrument in aiding the clinician in the diagnosis of patients presenting with murmurs of the heart.

The Cambridge Instrument Company kindly supplied a standard phonocardiograph outfit in every way similar to that used by Evans. It was decided to attempt a rough estimate of the suitability of this instrument by taking gross clinical examples of organic heart disease and subjecting them to phonocardiography, since it was considered axiomatic that the instrument must be able to record all the murmurs that could be heard on simple clinical auscultation. It was soon found that the standard instrument was incapable of recording the majority of relatively high pitched systolic and diastolic murmurs.

The Research Department of the Cambridge Instrument Company then kindly agreed to develop a modern apparatus from the new physical data that have been made available over the last twenty years; it was agreed that the clinical and scientific aspects should be closely co-ordinated. The apparatus is described later.

Those concerned with the visual recording of the heart sound vibrations must be grateful for the work of Rappaport and Sprague (1941 and 1942) in amplifying the basic data on which a reliable phonocardiograph should be constructed.

The heart sound vibrations are modified by the thoracic tissues as they radiate to the chest wall. This distortion will vary from person to person and is probably dependent largely on the amount of adipose tissue of the thoracic organs and of the chest wall itself and must remain an indeterminate variable in clinical phonocardiography.

Once the heart sound vibrations have reached the chest wall they are further modified for a clinician listening to the sounds with a stethoscope, by the stethoscope, which produces a certain degree of attenuation of sounds of low frequency, and by the human ear, which in the auscultatory range has a practically logarithmic low frequency attenuation response (see Fig. 2).

There are therefore three phonocardiographic records that may be considered physiological.

(1) A linear phonocardiogram. This is a visual record of the heart sound vibrations as they occur at the chest wall without any modification other than undistorted amplification, hence the term linear. The heart sound vibrations consist of an intense low frequency component (palpable but not audible) and a faint higher frequency component (audible). The linear phonocardiogram, however, resembles a jugular venous pulse record for it only shows the intense low frequency component. This component is 100,000 to 1,000,000 times more intense than the higher frequency vibrations which consequently cannot be shown on the same scale (see Fig. 9A and B, 11A and B, Part II).

(2) A stethoscopic phonocardiogram. This is a visual record of the heart sound vibrations from the chest wall as modified by an average stethoscope, that is as presented to the human ear. Such records will show low frequency events such as the third and fourth heart sounds as well as the whole range of murmurs and are the most generally useful phonocardiograms (see Fig. 4–8 and 10A and B, Part II).

(3) A logarithmic phonocardiogram. This is a visual record of (2) above, plus the additional modification of the average normal human ear. In other words it is a visual representation of the vibrations as presented to the sensorium of a listening clinician. The advantages of this type of record are firstly that its amplitude corresponds to the loudness heard by the clinician (a sound heard twice

as loud as another sound will be twice the amplitude of the other on the record); and secondly that as the low frequencies are extremely attenuated, a record taken from a patient with heart murmurs may be easier to interpret than one in which low frequency events are also recorded. Such a record should therefore be used to add to the information of a stethoscopic tracing (see Fig. 3, 9B, 10C, 11A and B, Part II).

It is necessary to record simultaneously some other manifestation of cardiac activity to provide a reference tracing for interpreting the phonocardiogram. The following tracings have been used for this purpose—the electrocardiogram, the subclavian or jugular venous pulse, the apex beat cardiogram and in special cases the arterial pulses.

The electrocardiogram has been used extensively because it can be recorded easily, but the only reliable reference point it gives is that mechanical ventricular systole never precedes the QRS complex of the electrocardiogram.

Since the electrocardiogram gives no reference points in diastole it is misleading to use it to determine the phase of the cardiac cycle of any diastolic event, either sounds or murmurs (see Fig. 5); it is, however, a valuable additional reference tracing to an apex beat or venous pulse recording, particularly when auriculo-ventricular dissociation is present or when there is some abnormality of propagation of the cardio-excitatory impulse.

The subclavian or jugular venous pulse gives, in addition to the onset of ventricular systole, the onset of auricular systole, the beginning of the second sound and a fair indication of the site of the third heart sound.

The apex beat tracing (linear phonocardiogram) gives the onset of ventricular systole, the beginning of the second sound and the third heart sound; it is as a rule easier to record by electrical means than the venous pulse and requires no time correction for vessel transmission of vibrations as does the venous pulse.

The heart sounds and most murmurs are noises in acoustic terminology, which means they are conglomerations of sound vibrations of various frequencies harmonically unrelated. In some cases, therefore, it is impossible to determine the exact onset of a murmur that follows a heart sound. Moreover, there is some variation in the vibrations recorded from one heart cycle to the next.

The Phonocardiograph

The apparatus used consists of a crystal microphone, a two-stage valve amplifier, and a Cambridge double-string Einthoven galvanometer. One fibre of this galvanometer is used for the electrocardiogram in the normal way; the other, which is used for the phonocardiogram, is tightened to its full extent in order to raise its high-frequency response. In this condition its sensitivity is about 1 mV/mm.

From examination of our phonocardiograms it will be noted that large excursions of the phonocardiographic fibre displace the electrocardiographic fibre. It has been proved experimentally that this is an air pressure phenomenon and not an electromagnetic interference, and that the phonocardiographic fibre is not affected by large excursions of the electrocardiographic fibre. The explanation of this effect lies in the greater sensitivity of the loose electrocardiographic fibre when it is calibrated for clinical use.

The microphone used is a Cosmocord Mic-6. This microphone was originally chosen because of its high sensitivity and high internal capacity. It has the disadvantage of being nearly 2 inches in diameter, so that good contact between the microphone and the chest is not always easy to attain. The sensitivity is stated by the makers to be about 10 mV/dyne/sq.cm. in the phonocardiographic frequency range.

The microphone is placed in a brass case which forms the chest piece. A ring of sorbo rubber is cemented to the case to assure good contact with a chest wall of irregular contour. The volume of the air chamber coupling the chest wall to the diaphragm is about 14 ml. The case is not intended to have any selective frequency properties; the intention is that the microphone and amplifier should have a fundamentally flat response, any other type of response being produced by controllable electrical filters in the amplifier.

The amplifier circuit is shown in Fig. 1. As the output has only to operate a string galvanometer the gain is not high, the voltage gain from the input to the galvanometer terminals being 100. A switched attenuator, placed between the two stages, controls the gain in steps of 2: 1, and a universal shunt connected across the galvanometer gives continuous control of gain at any setting of the attenuator. In phonocardiography, calibration of the controls is of little value, but they must cover a very wide range in order to deal with the varying levels of heart sound vibrations encountered.

In order to make the fundamental response as flat as possible, a 10-megohm resistor is placed across the microphone, which has a capacity of 0·002 μF. This gives a time constant of 0·02 second which, since it is the shortest time constant in the whole system, will control the low-frequency response; it should result in the response being down to half at about 8 c/cs. As explained later, such a response was not obtained.

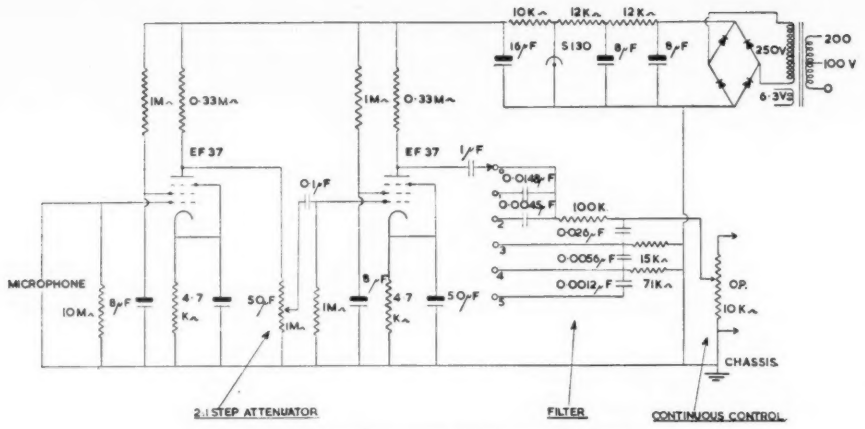

FIG. 1.—Amplifier circuit of phonocardiograph.

A 6-position filter, controlling the low-frequency response, is placed between the output stage and the galvanometer. At setting 0 the amplifier response is flat. At settings 1, 2 and 3 single-stage condenser-resistance filters, giving time constants of 0·0064, 0·002 and 0·0004 seconds respectively, are provided. These values give a loss of 3 db at 25, 80 and 400 c/s respectively, and a loss approaching 6 db/octave below these frequencies (stethoscopic phonocardiogram settings).

At settings 4 and 5, a 2-stage and 3-stage filter respectively are introduced, the time-constant of each additional section being 0·0004 seconds. These filters begin to cut off between 400 and 500 c/s (like that of setting 3) and give a loss approaching 12 and 18 db/octave respectively below these frequencies (logarithmic phonocardiogram settings).

Fig. 2 shows measured frequency responses for the assembly of microphone, amplifier, and galvanometer. These results were obtained by applying a variable frequency sound stimulus to the microphone with a pistonphone calibrator. Two points require comment. First, the low-frequency response at setting 0 is not flat; this is the result of accoustic leakage in the microphone assembly. The chief cause of this leakage is a felt ring which the makers fit round the rim of the microphone case. It is proposed in future to work without this ring, so that the response can be entirely controlled by the electrical circuit. Secondly, the response begins to fall above 500 c/s. This is the result of the galvanometer properties. The microphone has a resonance at about 2500 c/s, but the low galvanometer response at this frequency entirely masks this resonance. The high-frequency response attained is probably sufficient for the purposes of phonocardiography.

Conventional mains power supplies are provided. Rough HT stabilization is obtained by an S.130 gas tube, and the valve heaters are run on a.c. HT variations and heater pick-up are not unduly troublesome, but improvements in both these respects are desirable.

Special cable, type K.16 G.M. made by Telegraph Construction and Maintenance Co. Ltd., is used for the microphone input lead. This gives a very considerable reduction in the extraneous voltages produced when the microphone cable is moved in any way.

The advantages of a string galvanometer over other methods of recording high frequency phenomena are not great when an amplifier is essential. It was used in the research detailed in Part II because it was available. Comparative experiments have therefore been made with a double Duddell oscillograph, which has a wider frequency range and is more robust. This instrument, used in conjunction with appropriate amplifier circuits and a smaller microphone free from acoustic leakage, has been tried with promising results; Fig. 9A and B, 11A and B, Part II were taken with such an apparatus. The addition of an electrocardiographic channel is under consideration, but the whole of the apparatus is regarded as purely experimental at the moment.

The tracings are photographed at a speed which facilitates the accurate reading of phonocardiograms.

(References will be found at the end of Part II.)

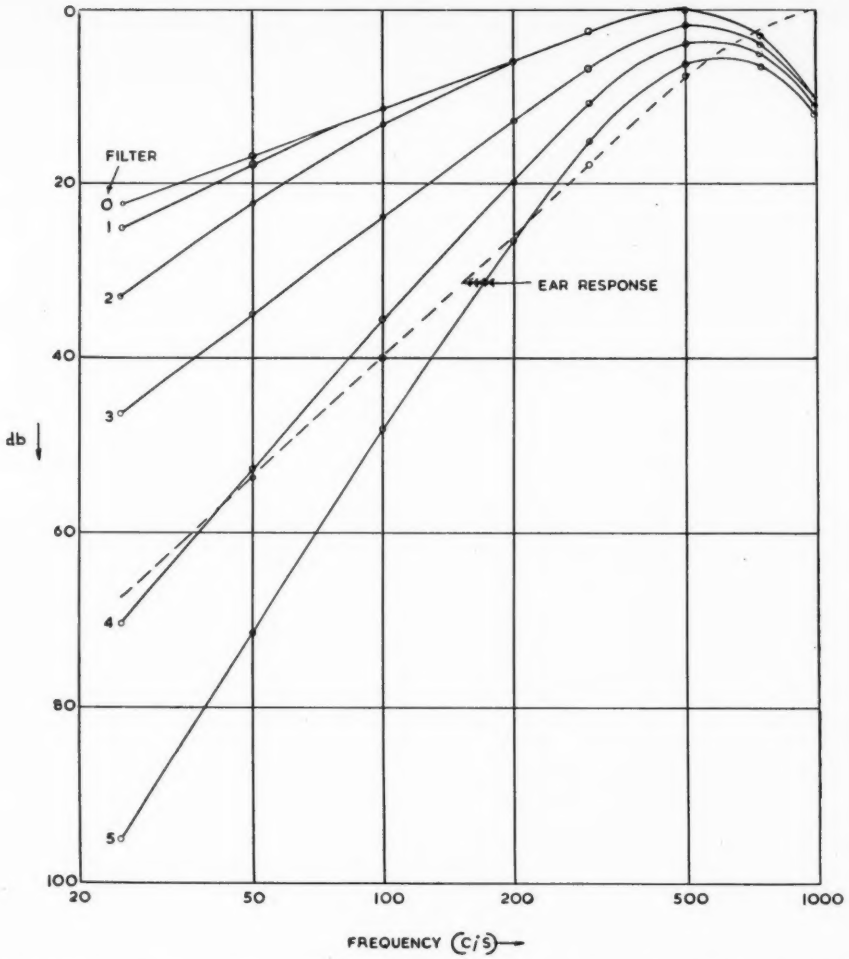

FIG. 2.—Frequency response curves of phonocardiograph and of "normal" human ear (audiogram).

THE PHONOCARDIOGRAPHY OF HEART MURMURS

PART II.—CLINICAL RESULTS AND DISCUSSION

BY

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Papers by William Evans (1947) suggested that the phonocardiograph could aid the clinician in the elucidation of the following points: (1) the distinction between the systolic murmur found with organic heart disease and the systolic murmur found with no organic heart disease, referred to as an innocent murmur; (2) the murmurs found in mitral stenosis; (3) the distinction between aortic incompetence of rheumatic as opposed to that of syphilitic ætiology; and (4) the presence of unsuspected aortic diastolic murmurs in cases of hypertension.

SYSTOLIC MURMURS

One important problem in clinical cardiology is the investigation of systolic murmurs in the hope that the healthy youngster with a systolic murmur can be saved from some form of cardiac invalidism imposed by the medical profession.

Evans (1947) found that the systolic murmurs in organic heart disease, with the exception of those found in hypertension, heart block, and a few cases of aortic valvular disease if recorded from the mitral area (which are all unimportant from the above standpoint), occur early in electrical systole; whereas the systolic murmurs recorded in subjects without clinical heart disease—the "innocent" group—occur in mid or late electrical systole.

Evans used the S line, a line drawn through the end of the S wave of lead II of the electrocardiogram to touch the simultaneously recorded phonocardiogram to distinguish the two groups. A systolic murmur occurring at the S line was found in the organic group while a systolic murmur beginning some distance after the S line was found in the innocent group. In none of the innocent group was a diastolic murmur recorded.

To investigate this point two series of cases were collected clinically and checked by cardioscopy and electrocardiography.

Group I consisted of 57 cases of known congenital or valvular heart disease with systolic murmurs to auscultation and phonocardiography (see Fig. 3–6, 8A, B, and C, 10A, B, and C).

Group II consisted of 27 cases with obvious systolic murmurs but with no other evidence of disease. An obvious systolic murmur has been taken as one lasting an appreciable interval into systole between the first and second heart sounds and of not less than moderate intensity (Grade III, Levine, 1945), for it is this group of murmurs that presents a clinical difficulty as to whether organic disease is present or not. In four cases the systolic murmur was loud or very loud (Grade IV or V) and one of these suffered an undoubted attack of subacute bacterial endocarditis after the investigation—emphasizing that an organic lesion was present although careful cardiological investigation revealed no deviation from the normal other than a loud systolic murmur. Twenty-one of these cases (77 per cent.) were aged 30 or under. (See Fig. 7A, B, and C).

The phonocardiograph employed recorded a stethoscopic or logarithmic phonocardiogram with lead II electrocardiogram as reference tracing. (See Part I.) The time-marker on all the records is 0·2 seconds. Records are marked to show the

TABLE I

RELATION OF ONSET OF SYSTOLIC MURMURS TO S LINE IN LEAD II ELECTROCARDIOGRAM

Timing	Valvular or congenital heart disease 57 cases		No diagnosed heart disease 27 cases	
After S ..	38	66·6%	27	100%
At S	9	15·7%	—	—
Doubtful ..	10	17·5%	—	—

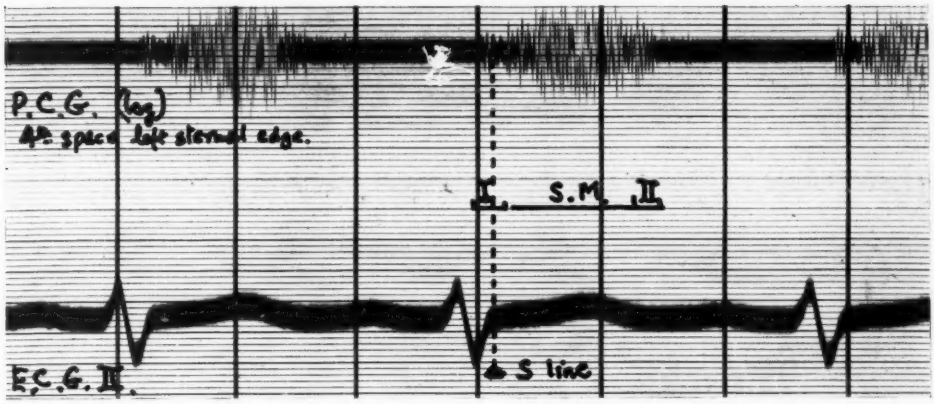

FIG. 3.—Ventricular Septal Defect. Logarithmic phonocardiogram from site of maximal intensity of murmur—note that low frequencies in the first and second heart sounds are not recorded, and that the base line is very clear.

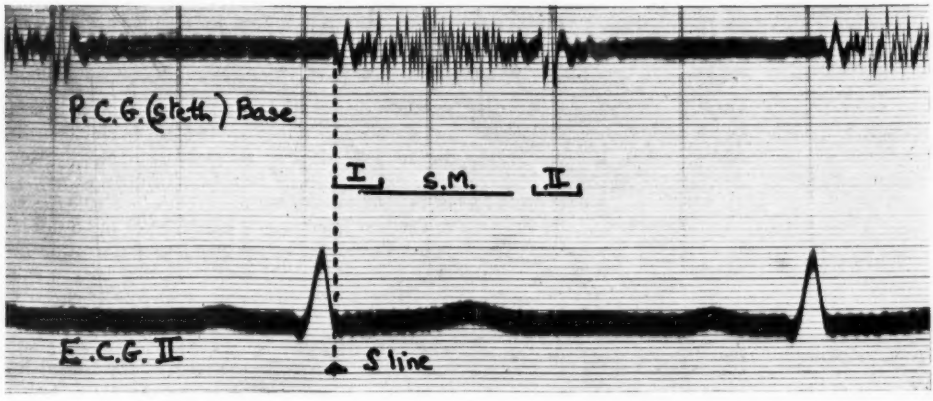

FIG. 4.—Aortic stenosis. A second heart sound was audible at the base and is recorded.

S line, the heart sounds I, II, III, and IV, systolic murmurs (S.M.), and diastolic murmurs (D.M.). Other lettering is explained under the appropriate figure. The site from which the record has been taken is indicated after the type of phonocardiogram shown (steth = stethoscopic, log = logarithmic).

It will be seen that in two-thirds of the organic cases the systolic murmur began after the S line, whereas only in 9 did it begin at the S line. A further analysis (Table II) of these 9 cases shows that a systolic murmur occurring at the S line can occur with most forms of valvular or congenital heart disease but wherever there were sufficient cases to draw any conclusions it appears to be uncommon in any particular defect. (See Fig. 8A).

It would appear from this investigation that the systolic murmurs encountered in valvular and congenital heart disease cannot be differentiated from the systolic murmurs occurring with no recognizable heart disease by their relation to the S line of lead II of the electrocardiogram. For although in all the Group II cases the systolic murmur occurred after the S line, the same applied to at least 66 per cent of the cases in Group I.

It has been known for many years that mechanical and electrical systole in man and experimental

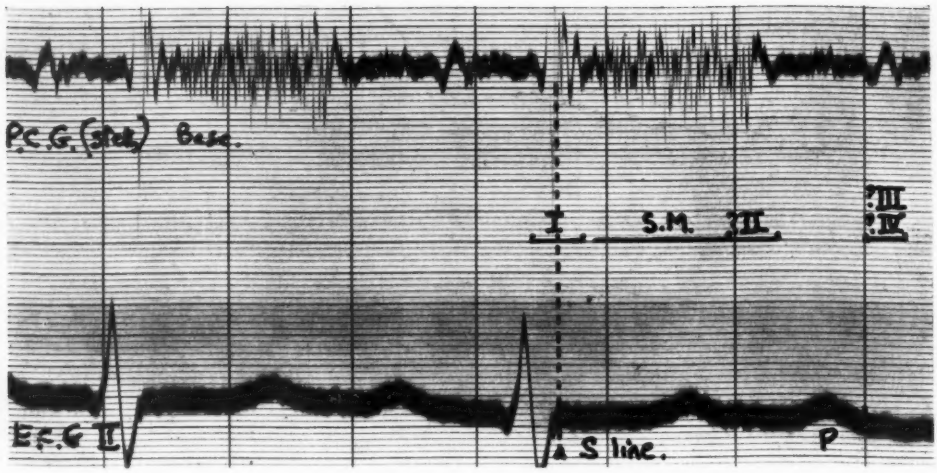

FIG. 5.—Pulmonary stenosis. No second heart sound was audible or is recorded. Record shows a low frequency event marked ?III ?IV which could be either a third heart sound because it occurs about 0·2 sec. after the second heart sound, or a fourth heart sound occurring as it does just after the P wave of the electrocardiogram, or a combination of both. The electrocardiogram cannot be used to differentiate these possibilities.

TABLE II

ANALYSIS OF RELATION OF ONSET OF THE SYSTOLIC MURMUR TO THE CLINICAL DIAGNOSIS IN ORGANIC HEART DISEASE

Diagnosis	Site of record	No. of cases with S.M. at S line	No. of cases with S.M. after S line	No. of cases with doubtful onset of S.M.
Aortic incompetence	Base	3	12	3
Aortic stenosis ..	Base	1	1	0
Mitral stenosis ..	Apex	1	11	2
Combined rheumatic valvular lesions	Apex	1	5	2
Active rheumatic carditis	Apex	1	0	0
Auricular septal defect	Base	1	0	2
Ventricular septal defect	4th space left sternal edge	1	2	1
Pulmonary stenosis..	Base	0	3	0
Fallot's tetralogy ..	Apex	0	2	0
Patent ductus arteriosus	Base	0	1	0
Lutembacher's syndrome	Apex	0	1	0
Total	57	9	38	10

animals are not simultaneous either in onset or in duration (Wiggers, 1944). Such asynchrony would provide the simplest explanation for the varying relation of systolic murmurs to the S line of the electrocardiogram. Thus in Fig. 4 the whole of the first heart sound occurs after the S line.

It will also be noted that it is a condition of the cases in Group II that they should have a normal electrocardiogram, whereas many cases in Group I had abnormal electrocardiograms often with a widened QRS interval. However, only 3 of the 9 cases with a systolic murmur at the S line had a widened QRS interval.

MITRAL STENOSIS

Evans (1947) found that when a systolic murmur was heard without a presystolic murmur in mitral stenosis, the murmur as recorded by phonocardiography started during the P–R period of lead II of the electrocardiogram in 33 out of 41 cases. In other words the murmur was really presystolic and not systolic in timing and due to auricular contraction. He also found that the systolic murmur never occurred later than the S line and that there was a mid-diastolic murmur in all of his 74 cases.

To test these points a consecutive series of 30 cases of mitral stenosis was investigated. (See Fig. 8A, B, and C.) In 17 of these cases a systolic murmur was recorded as it was heard. It never occurred

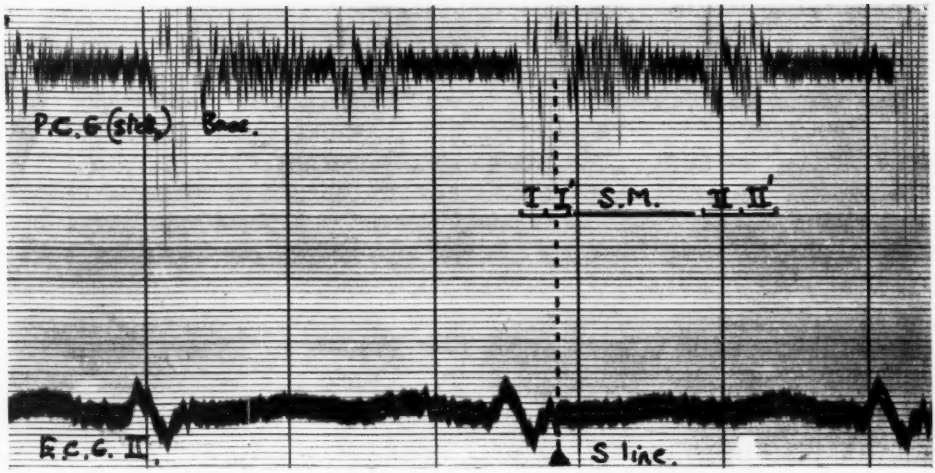

FIG. 6.—Atrial septal defect. Note splitting of the first and second heart sounds. This is not a good record as it shows "mush."

during the P–R period of the electrocardiogram. In all 17 it occurred after the first heart sound. Its relation to the S line lead II electrocardiogram was as follows:

After the S line in	12
At the S line in	2
Exact onset doubtful in	3

In 15 of the series a presystolic murmur was heard, and in all 15 cases it was clearly seen on the record during the P–R period of the electrocardiogram. It was always separate from a systolic murmur if present and also differed from such a systolic murmur in that its mean frequency was considerably lower (See Fig. 8C.)

The position of the second heart sound in Fig. 8A and B has been determined by taking phonocardiographic records from the base of the heart where the second sound was clearly seen in these cases and transposing to the apical records. Apical and basal records were taken within a few minutes of one another. (Fig. 10A is a record from the base of the heart and Fig. 8A an apical record in a case of combined mitral stenosis and aortic incompetence.) The second heart sound is probably split in Fig. 8C.

It is my impression that the sole information which the phonocardiograph has added to that of auscultation in the cases of mitral stenosis in this series is that a mitral diastolic murmur occurs more frequently than it is heard. However, one cannot be certain of this unless the record shows a clear base line, and this was not always obtained.

Problems such as whether an opening snap of the mitral valve is always present in mitral stenosis, and the differentiation of this snap from a third heart sound (which may be of diagnostic importance in mitral stenosis) could not be investigated owing to the limitations imposed by the apparatus in having no other reference tracing than the electrocardiogram. Fig. 9A is an apical record from a case of mitral stenosis, with a linear phonocardiogram (apex cardiogram) as reference tracing in which a third heart sound is clearly indicated and in which no opening snap of the mitral valve is shown.

AORTIC INCOMPETENCE

Evans, in a series of 20 cases of aortic incompetence, found that 8 were clinically of syphilitic ætiology and 12 of probable rheumatic origin, although with no definite evidence of this after full cardiological investigation. After phonocardiography at the apex he considered that there was proof of rheumatic ætiology in 16 out of the 20 cases because of the presence of presystolic and mid-diastolic murmurs from added mitral stenosis.

To test this finding a series of 21 consecutive cases of aortic incompetence was investigated clinically (see Fig. 10A, B, and C); 11 were considered to be of rheumatic, 5 of syphilitic, and 5 of unknown ætiology.

Of the 11 rheumatic cases, 5 had definite evidence of mitral stenosis both to clinical and to phonocardiographic examination (See Fig. 10A and 8A taken from same patient.) In the remaining 6

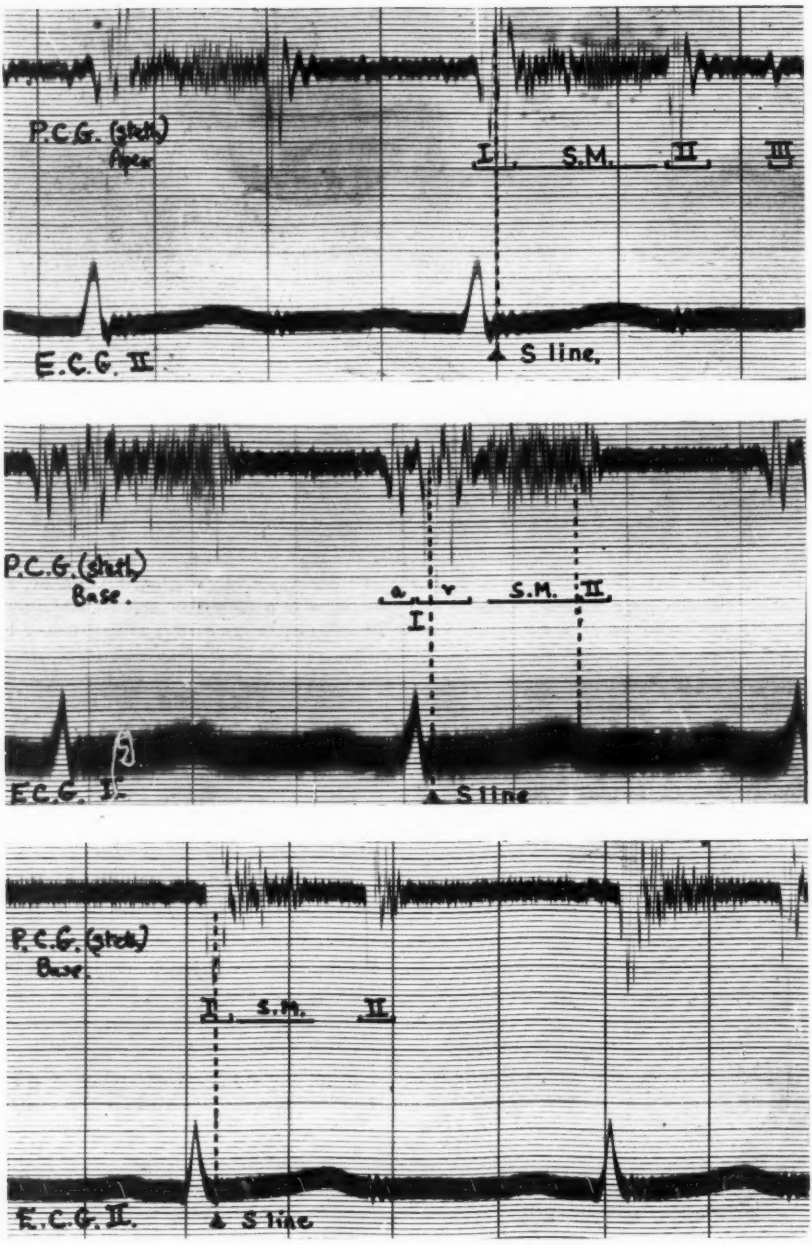

FIG. 7.—"Innocent" systolic murmurs. Note that the relation of the systolic murmur to the S line does not differ from that found in organic heart disease.
In (B), note the auricular part of the first heart sound (a).

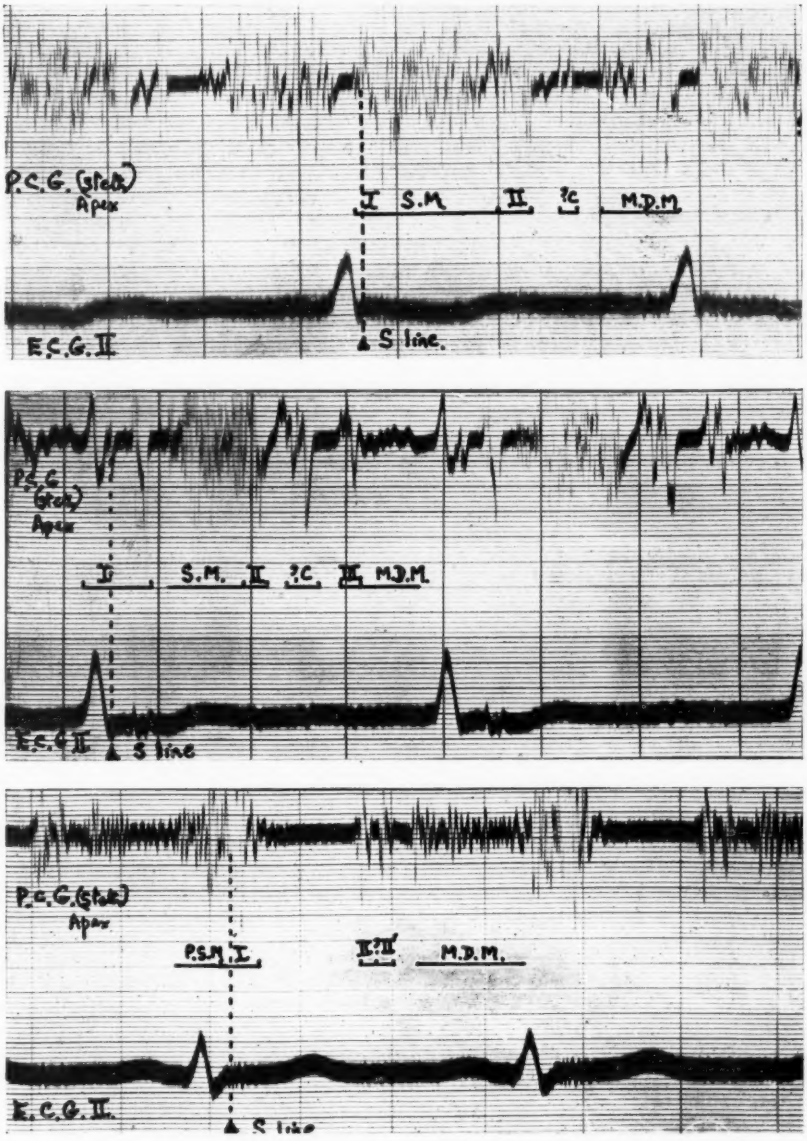

FIG. 8.—Mitral stenosis—apical recordings. Three patients.
(A) Systolic murmur (S.M.) starting at the S line.
(B) Systolic murmur starting well after the S line.
(C) No systolic murmur.

A presystolic murmur (P.S.M.) is only shown in (C), auricular fibrillation being present in (A) and (B).

The opening snap of the mitral valve is probably shown at (c) in (A). Mid-diastolic murmur (M.D.M.).

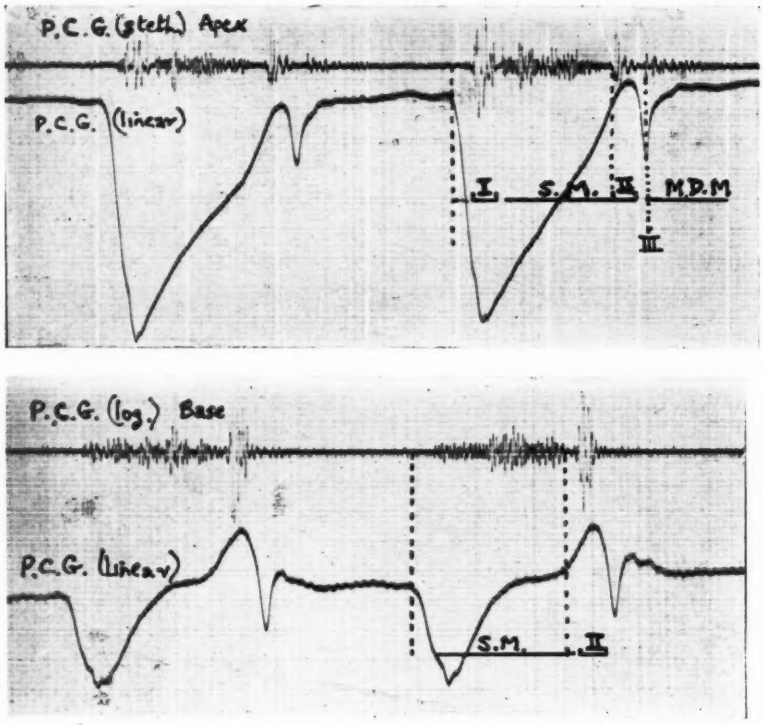

FIG. 9.—Mitral stenosis. (A) Apical and (B) basal records of one patient. A loud pulmonary second sound was heard and the large amplitude of this sound in the logarithmic basal record is well seen.

cases there was no auscultatory or phonocardiographic evidence of mitral stenosis, although in 2 of these the apical records showed long aortic diastolic murmurs that might have obscured any mitral mid-diastolic murmurs present.

Of the remaining 10 cases in the series, none showed phonocardiographic evidence of mitral stenosis although 4 had long aortic diastolic murmurs recorded on the apical records, which might have obscured any mitral mid-diastolic murmurs present.

One case with aortic incompetence and subacute bacterial endocarditis, but of uncertain ætiology, in which no evidence of mitral stenosis had been heard or recorded by phonocardiography, died. Post-mortem, no enlargement of the left auricle was found; there was no evidence of rheumatic endocarditis or valvulitis, and microscopy did not elucidate the ætiological diagnosis.

In this series of cases of aortic incompetence no additional information to that found on clinical examination was given by phonocardiography.

Unsuspected Aortic Diastolic Murmurs in Hypertension

Evans found aortic diastolic murmurs in 12 of a series of 43 hypertensive cases and in some cases of heart block. In order to test this finding a series of 20 cases of hypertension with loud or ringing aortic second sounds and diastolic blood pressures consistently over 100 mm. was investigated. In no case was a diastolic murmur heard clinically. The ringing quality as heard by auscultation showed itself as a musical second sound of no greater width than normal on phonocardiographic records taken from the aortic area, and no diastolic murmur was detected after the second sound in any case (See Fig. 11A and B.)

Evans in interpreting his records has stated that "at the end of the T wave (lead II electrocardiogram) the second sound starts." Such a relationship has not been observed by other users of the phonocardiogram (Orias and Braun-Menendez, 1939). It can be seen from Fig. 7B and 10B that

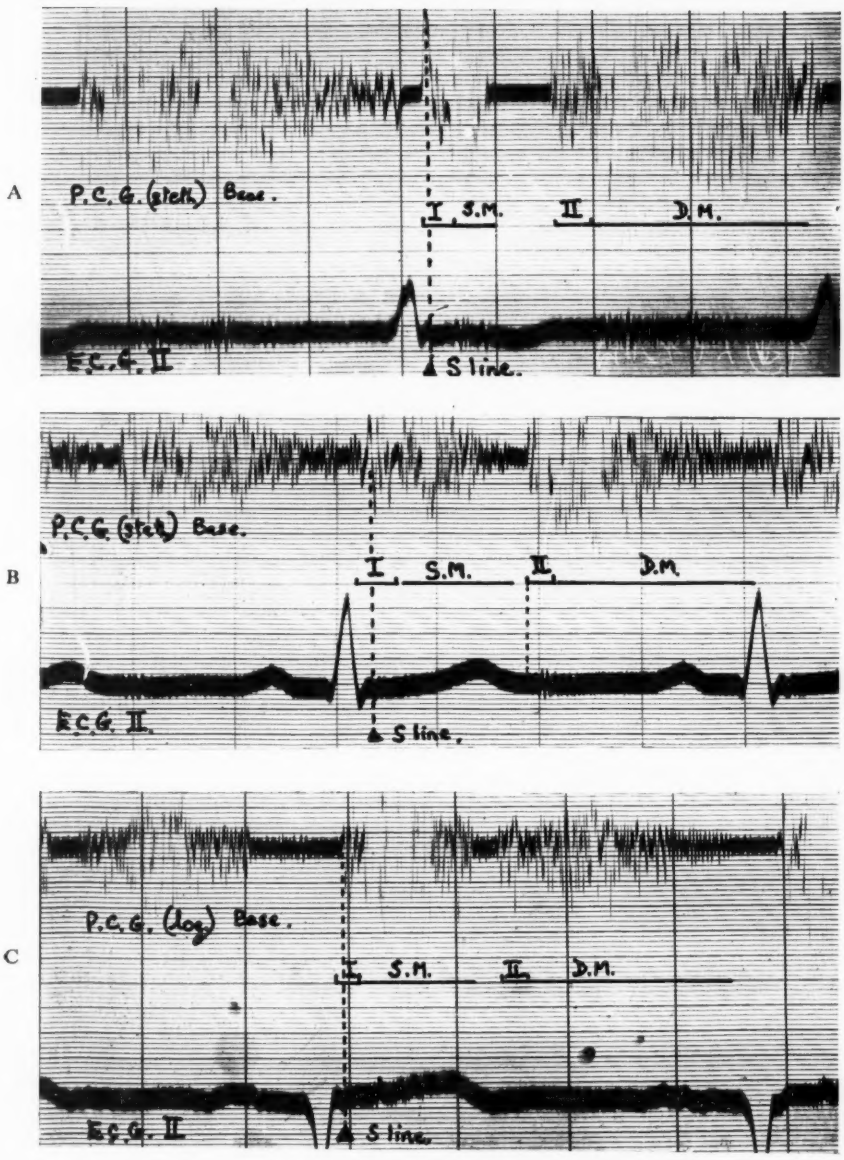

FIG. 10.—Aortic incompetence—basal recordings. Three patients. (A) and (B) are stethoscopic and (C) a logarithmic phonocardiogram.

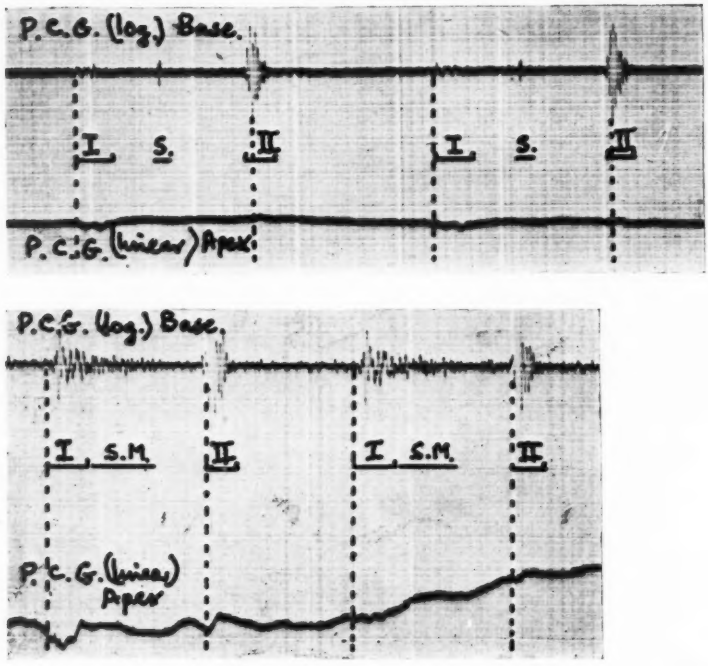

FIG. 11. Hypertension—basal recordings. Two patients. Ringing aortic second sounds but no diastolic murmurs are present. A systolic gallop sound (S) is present in (A).

the T wave bears a sufficiently variable relationship to the second sound to make it valueless as an indication of the onset of the second heart sound. It is believed that Evans' records of hypertension can bear a different interpretation if this is taken into account.

SUMMARY AND CONCLUSIONS

An investigation was planned to test some of the phonocardiographic findings on heart murmurs announced by Evans (1947). In order to do this it became necessary to construct a new phonocardiograph whose characteristics are described in Part I.

No clear-cut distinction between the systolic murmurs found in valvular and congenital heart disease (57 cases) and those found in patients with no evidence of heart disease (27 cases) could be established by timing the onset of these murmurs against the S line of lead II of the electrocardiogram.

The systolic and presystolic murmurs in 30 cases of mitral stenosis were found to be clearly distinguishable from one another in timing and mean frequency, as they were on clinical auscultation.

No additional ætiological information to that collected clinically was found by a phonocardiographic examination of 21 cases of aortic incompetence.

In 20 cases of hypertension with a consistent diastolic blood pressure of over 100 mm. none was found with an aortic diastolic murmur.

For phonocardiography to be a useful aid in clinical cardiology it is necessary to use an instrument whose characteristics are known and satisfy certain basic considerations. The electrocardiogram alone is an unsatisfactory reference tracing for studying heart murmurs by phonocardiography as there is no strict co-relation between the electrical and mechanical events of the cardiac cycle.

Although the phonocardiographic investigations recorded in this article are of a negative nature it is felt that phonocardiography can help the clinician in the diagnosis of heart murmurs, and work on these lines is progressing.

It has been a great pleasure to work in close co-operation with the Research Department of the Cam

bridge Instrument Company, England, to whom my grateful thanks are offered.

I wish to record my thanks to Professor Sir Lionel Whitby, Regius Professor of Physic at Cambridge, for much help and advice; to Dr. Leslie B. Cole of Addenbrooke's Hospital, Cambridge, for permission to use his cases and for his enthusiasm and advice; and to Dr. William Evans for his generous advice and help.

This work was undertaken during the tenure of an Elmore research studentship at the University of Cambridge.

References

Evans, W. (1947). *Brit. Heart J.*, **9**, 1 and 225.

Levine, S. A. (1945). *Clinical Heart Disease*, Philadelphia.

Orias, O., and Braun-Menendez, E. (1939). *The Heart Sounds in Normal and Pathological Conditions*, London.

Rappaport, E. E., and Sprague, H. B. (1941). *Amer. Heart J.*, **21**, 257, and (1942), *ibid.*, **23**, 591.

Wiggers, C. J. (1944). *Physiology in Health and Disease*, London.

THE NATURAL HISTORY OF CORONARY DISEASE

A CLINICAL AND EPIDEMIOLOGICAL STUDY

BY

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Since William Heberden wrote his classic account of angina pectoris in 1768 and Edward Jenner, in a letter to him ten years later, suggested the association of the syndrome with disease of the coronary arteries, the subject has continued to claim the interest and attention of physicians in each succeeding generation. Taking this country alone and excluding living authorities, we have only to recall such names as Latham, Clifford Allbut, Osler, Mackenzie, and Lewis. Symptomatology, both in their periods and since, has been the chief object of speculation and of study and although, with the aid of a more refined and intimate case-work, the subjective phenomena could even now be accorded a more detailed and accurate portraiture, the general clinical picture has been widely approved. The physiological researches of Lewis and his colleagues have advanced our understanding of the pain which is the central symptom. Morbid anatomy (especially in its bearing upon coronary occlusion as the cause of the status anginosus and succeeding cardiac failure), cardiography and radiography, have all made their contributions. Prognosis, with the assistance of technical aids and in experienced hands, has achieved, perhaps, a slightly better precision. Therapeutics, except insofar as a number of useless remedies have been discarded, have not registered any outstanding gains since Lauder Brunton's advocacy of the nitrites. The course of the disease *in individuals* and the effects of symptomatic treatment have, in brief, been fairly adequately covered.

The study of the disease *in the community*, on the other hand—its epidemiology and ætiology—have scarcely as yet received adequate consideration. Where individual studies leave gaps in our knowledge social and statistical enquiry may have a contribution to make.

When Heberden, who had no hospital associations, gave his paper to the Royal College of Physicians his experience of angina pectoris amounted to some 20 cases. When he included the description in his "Commentaries" in 1782, his experience had extended to 100 cases. Osler was admitted to the Fellowship of the Royal College of Physicians before he had seen a case in hospital or private practice. Mackenzie, with all his earlier experience in general practice and later as a leading consultant in cardiology, wrote (as late as 1923) that 380 patients had consulted him for angina pectoris. Today, as Cassidy (1946) remarks, "the modern cardiologist's name is legion" and "he counts his cases by thousands rather than hundreds." On both sides of the Atlantic the steadily rising incidence of coronary disease in recent decades has been noted, and it has been suspected that this trend, as indicated by mortality figures, is not wholly to be explained by such factors as the changing age-constitution of populations and by improved diagnosis and certification at death.

In connection with ætiology, speculations have been frequently advanced concerning the influence of the manifold stresses inherent in the conditions of life and work that our industrial civilization has imposed, and concerning the possible effects of nicotine. That hereditary predisposition plays some part has long been allowed. The assumption that angina pectoris and coronary occlusion are, in the main, expressive of nothing more than the arterial degenerations that accompany the inescapable process of "ageing" has not seemed satisfactory in the absence of a definition of ageing and in the case of a disease so common at the summit of a man's energies and achievement, and now so frequently recorded in the fifth and sixth decades (i.e. at ages 40–59), not infrequently in the fourth decade (30–39), and sometimes even earlier (20–29). Adherents of the so-called psychosomatic school of medicine—perhaps beause their approach has been too predominantly psycho-analytical and because they have tended to see selected examples rather

than the general run of cases that pass through the hands of the family practitioner, the physician and the cardiologist—have almost certainly overstressed the influence of specific emotional conflict. Those cardiologists, on the other hand, who have doubted the ætiological contributions of mental stress and fatigue, with or without the addition of the more ordinary types of day-to-day anxiety, may be shown to have erred in another direction and to have attached altogether too little importance to the body-mind relationship and to the exacting circumstances of modern modes of life and work, which are in many respects as different as it is possible to imagine from those enjoyed or endured by our more slowly moving agricultural forebears.

The Scope of the Enquiry

The present study falls into two parts. The first is based upon a statistical analysis of material to be found in the Reports of the Registrar-General (covering a recent twenty-five year period) in its bearing upon the deaths from coronary disease in England and Wales. This study has involved correlations with age, sex, social class, and occupation and geographical distributions, and has taken into particular account the secular trend of the disease during the period under review. The second is based upon an analysis of the clinical histories of a series of cases seen by one of us (J.A.R.) during a closely similar period of 23 years in the course of consulting practice.

In this manner, and by pooling our experience, it seemed to us that we could, in some measure, combine the advantages of two of the more important methods of socio-medical enquiry. *Statistical surveys* with correlations based upon official mortality returns rely for their validities upon the large numbers employed. While recognizing that the original data upon which the figures are based have been subscribed by a host of observers of varying reliability, we may yet accept that there is a sufficient smoothing out of error, by virtue of quantity, to compensate for qualitative inaccuracy. As regards the diagnosis of most cases of fatal angina pectoris and coronary occlusion in the period covered by the statistical survey, there should not have been great difficulties, so familiar had the symptom-picture of the first stage of the disease and, commonly, of the second stage, by then become. Nevertheless, steps were taken, as will be seen, to meet the criticism that the diagnosis of coronary thrombosis or occlusion has been made with increasing frequency throughout the period under review, and that certain vague nomenclatures, such as " myocardial degeneration " (which have long been loosely used in death certificates) must now be giving place to more accurate classifications and thereby accounting in large part for the increased rates of mortality.

A *clinical survey*, even when conducted in retrospect—given that sufficient attention has been paid to possible personal, familial and habitual influences and to social and occupational factors and to the age at onset of the disease—has some, but only some, of the merits of a planned socio-medical enquiry. As a study in morbidity (and this is especially so in the case of diseases that run a long course) it may be considered as a useful supplement to mortality studies, for these can give no indication of age at the onset of the symptoms or of the conditions of life and work then obtaining, and they cannot, as a rule, attempt correlations with other ætiological factors than sex, social class, occupation, and geography. Nor can they throw light upon the various durations of the disease. As a rule, however, the numbers available for a personal clinical study of this kind are very small by comparison with those required by the statistical epidemiologist and often some necessary evidence is found to have been omitted or recorded in a form unsuitable for abstraction. Conclusions drawn from the physician's numerical analyses must consequently be cautious. The majority of cases in the clinical series were seen on one occasion only; some on two, three or more occasions; a few were seen so often and over such long periods of time as to allow of a growing intimacy both with the manifestations and varied course of the malady and with the affairs and personalities of its victims. An obvious disadvantage of the series relates to the fact that the cases were, inevitably, socially selected. An advantage, on the other hand, may be discerned in the fact that the information was collected by a single observer, and that his interest at the time was concentrated on the whole disease rather than upon any particular aspect of it.

The Statistical Study

In 1926 the reported deaths from angina pectoris in England and Wales totalled 1,880. In 1945 the number of deaths ascribed to disease of the coronary arteries and angina pectoris was 25,012, of which 16,514 occurred among males and 8,498 among females. During the intervening years the mortality from this cause of death has steadily increased and, in this connection, the comment by the Registrar-General (text for the years 1938–9) is of interest:

> " The progressive increase since 1920 in the standardized mortality assigned to coronary disease and angina pectoris continued without a break in 1938 and 1939. In 1920 the rates were

32 per million for males and 13 for females, and by 1939 they were twelve or thirteen times as great (406 and 153 respectively). To what extent this increase is explained by changing fashion in death certification, leading to transfer of deaths from myocardial and cardiovascular degeneration groups, and to what extent it is real, is difficult to ascertain."

The present study, based on the statistics relating to the period 1921–45, was undertaken with the aim of attempting to shed some light on the increased mortality from coronary disease and to observe its social and geographical distribution in England and Wales and its sex relationship.

If the increment that has ostensibly occurred in the mortality has been obtained at the expense of the myocardial group, it is important that the composition of these groups should be uniform or stable during the period of observation. In the present study the following sub-headings and their attached numerical identification in the list of the International Classification of Causes of Death were adopted as suitable criteria:

	Period	*Sub-headings*
Myocardial group	1921–30	Fatty heart 90 (5)
	,,	Other or unspecified myocardial diseases 90 (7)
	,,	Arteriosclerosis without record of cerebral vascular lesion 91 (b) (2)
	1931–9	Myocardial degeneration 93 (b)
	,,	Myocarditis not distinguished as acute or chronic 93 (c)
	,,	Arteriosclerosis without record of cerebral vascular lesion 97 (3)
	1940–5	Myocardial degeneration, infarction, sclerosis and other chronic myocarditis 93 (c)
	,,	Myocarditis not distinguished as acute or chronic 93 (d)
Coronary disease	1921–30	Angina pectoris 89
	1931–9 and 1940–5	Diseases of the coronary arteries, angina pectoris 94

Secular Trend

In discussing the secular trend of the mortality from any disease or disease-groups over a long series of years, it is essential to be mindful of difficulties that do arise. These may be listed as follows:

(a) Changing fashion in diagnosis.

(b) Changes in the International Classification of Causes of Death.

(c) The abandonment by the Registrar-General of a priority classification and his acceptance of the sequence as stated by the doctor when more than one cause of death is mentioned on the death certificate.

While allowance has been made by the Registrar-General for the influence of (b) and (c) in statistics published for years since 1931, the impact of (a) remains an unknown quantity. There also exists another influential factor in the trend of the all-ages mortality, namely the effect of change in the age composition of the population. The extent to which this has occurred, even during the relatively short period under review, is manifest in the following figures indicating the proportional age distribution of the population in 1921 and 1945.

TABLE I

CHANGING AGE OF POPULATION

Year	Age groups				All ages
	0–14	15–44	45–64	65+	
1921 pop. ..	29	47	18	6	100
1945 ,, ..	21	46	23	10	100

The proportion of the population in the age group 45–64 years increased by nearly 30 per cent, and at age 65+ by nearly 70 per cent, during this time interval of 25 years. It is possible to make allowance for the influence of the ageing factor on the death-rate by calculating the comparative mortality index. This index, which was devised by Dr. Percy Stocks, " expresses each cause of mortality of each year as a ratio of that of 1938 adopted as the base after adjustment for age differences in the population exposed to risk."

Since the diseases that are being studied occur in adult life, and predominantly after the age of 30, the index, in the present instance, was calculated for age 35 years and upwards. The results for the period 1921 to 1939 for males and females are shown in Fig. 1 and 2, to which was added, as a matter of interest, the curve of the mortality from arteriosclerosis with a record of cerebral vascular lesion.

The upward direction of each of the curves is quite a definite feature of the graphs, but, for both sexes, the gradient is steepest for coronary disease. If three points of time be taken—1921, 1931, and 1939—the comparative mortality index for coronary disease for males was 0·10, 0·47 and 1·13; the corresponding values for females were 0·09, 0·42 and 1·08. The graphs also reveal:

(1) The very close alignment between the trend of the mortality from the myocardial group and arteriosclerosis, particularly for females.

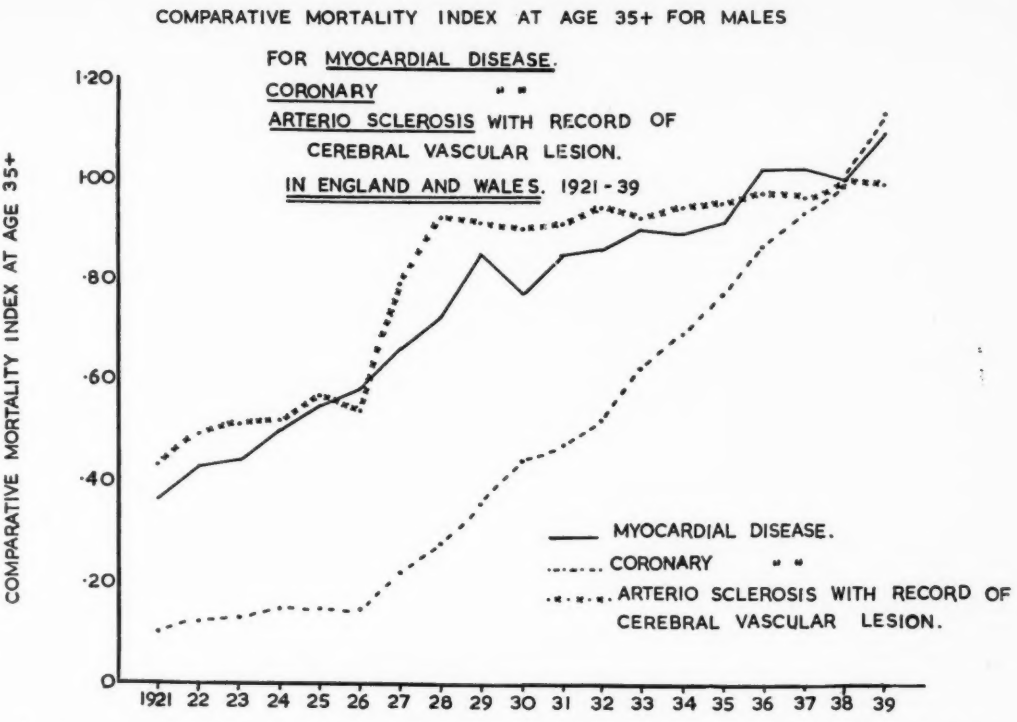
COMPARATIVE MORTALITY INDEX AT AGE 35+ FOR MALES
FOR MYOCARDIAL DISEASE.
CORONARY " "
ARTERIO SCLEROSIS WITH RECORD OF CEREBRAL VASCULAR LESION.
IN ENGLAND AND WALES. 1921-39
COMPARATIVE MORTALITY INDEX AT AGE 35+
1·20
1·00
·80
·60
·40
·20
0
1921 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
MYOCARDIAL DISEASE.
CORONARY " "
ARTERIO SCLEROSIS WITH RECORD OF CEREBRAL VASCULAR LESION.

FIG. 1.—Comparative mortality index at age 35+ for males for myocardial disease, coronary disease, and arteriosclerosis with record of cerebral vascular lesion, in England and Wales 1921–39.

(2) The increment in the death-rate from arteriosclerosis with a record of cerebral vascular lesion between 1926 and 1928, an increase so great and so abrupt as to suggest that it indicates a change in "book-keeping" rather than anything specific in the disease itself.

Since the progressive increase in each of the three causes of death is evident, it is pardonable to make a digression here to ascertain if such increment has been due to a transference of deaths from other forms of circulatory disease. On this particular issue the following statistics, published by the Registrar-General in the text of the report for the years 1938–9, are instructive. As regards the male mortality, which is the more important, the increment in the death-rates at ages when circulatory disease is classified into two groups, A and B, was as shown in Table II.

TABLE II

INCREASE (+) OR DECREASE (−) IN RATES PER MILLION FROM 1921–30 TO 1939

Age group	(A) Coronary. Myocardial. Arteriosclerosis. Senility	(B) Valvular and "other heart" disease
	Males	Males
45—	+581	−284
50—	+1377	−369
55—	+2420	−737
60—	+4110	−1477
65—	+6114	−2806
70—	+9674	−3994
75+	+20856	−5861

The figures suggest that some transference may have occurred from B to A, but certainly not sufficient to account for the vast increase observable in the latter. To quote the Registrar-General: "Such transfer could, however, account for only a fraction of the increase registered amongst males for degenerative diseases affecting the myocardium and vascular system." The position would thus seem

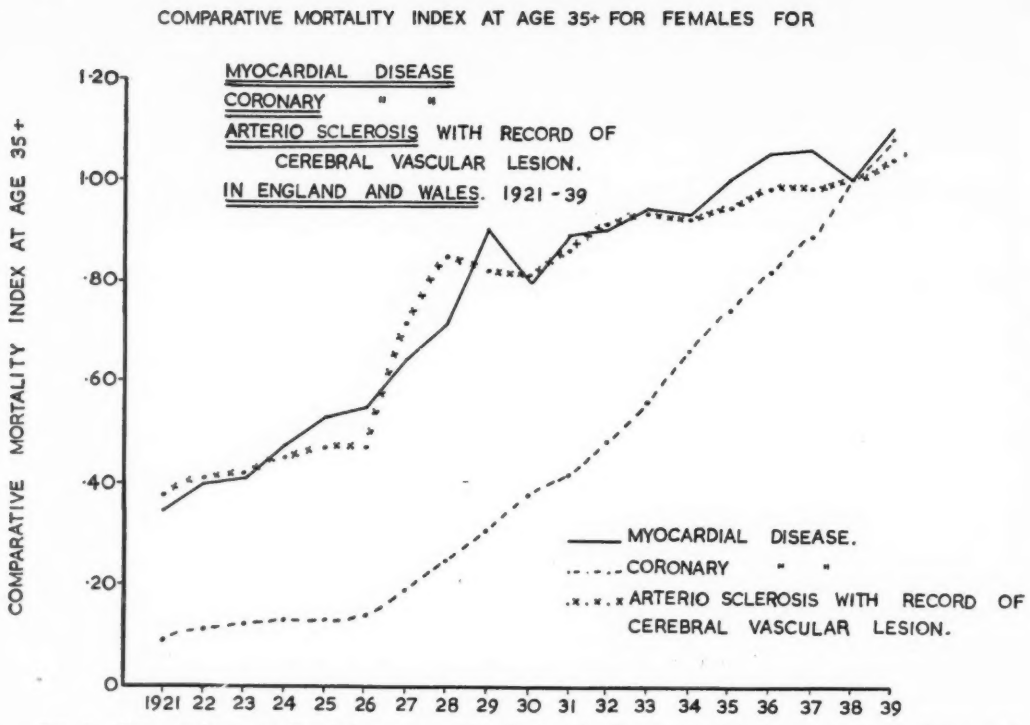
COMPARATIVE MORTALITY INDEX AT AGE 35+ FOR FEMALES FOR
MYOCARDIAL DISEASE
CORONARY " "
ARTERIO SCLEROSIS WITH RECORD OF CEREBRAL VASCULAR LESION.
IN ENGLAND AND WALES. 1921-39
COMPARATIVE MORTALITY INDEX AT AGE 35+
1·20
1·00
·80
·60
·40
·20
0
1921 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
MYOCARDIAL DISEASE.
CORONARY " "
ARTERIO SCLEROSIS WITH RECORD OF CEREBRAL VASCULAR LESION.

FIG. 2.—Comparative mortality index at age 35+ for females for myocardial disease, coronary disease, and arteriosclerosis with record of cerebral vascular lesion, in England and Wales 1921–39.

to be that, up to 1939, coronary and myocardial disease were each increasing but not doing so mainly at the expense of the residual circulatory forms, and that the rate of increase was much greater in respect of the mortality from coronary disease. But the similarity in the trend of the respective mortality of the two disease-groups ended in 1939 because the subsequent statistical experience, especially since 1941, has been entirely different. The comparative mortality index for coronary disease in males in 1945, was 1·43, or 43 per cent greater than the death-rate in 1938, whereas the myocardial index was 0·76, or 24 per cent in defect of the 1938 standard. Similarly for females, the 1945 index for coronary mortality was 1·38, or 38 per cent greater than that in 1938, but the myocardial ratio was 0·80, or 20 per cent in defect. It would thus seem that there has been either (a) a real decrease in myocardial mortality, or (b) a change in certification, observable since 1940; and that some deaths, previously attributed to myocardial causes, are now ascribed to one or other of the circulatory forms. The divergence in point of time is too abrupt and sudden to indicate (a); and (b) would therefore offer the more sensible explanation.

Mortality According to Age

(i) *Coronary disease.* While a picture of mortality based on a rate or ratio for combined ages, even though such values be adjusted for effects of ageing of the population, is informative, it nevertheless lacks the clarification that a study of age-specific rates of mortality can afford. For this reason the average annual death-rates in age groups from coronary disease in the periods 1921–30, 1931–39 and 1940–45 (excluding 1944), and the percentage increments relative to the first epoch, are given in Table III. The death-rates at ages in the periods 1921–30 and 1931–39 were adjusted (by the application of conversion ratios) so as to make them comparable with those based on the revised classification that became operative in and after 1940. In the interpretation of the results it is essential to bear in mind that the time intervals are different,

TABLE III

THE DEATH-RATES PER MILLION OF POPULATION IN AGE GROUPS FOR CORONARY DISEASE IN ENGLAND AND WALES FOR CERTAIN PERIODS

Coronary Disease

Age group	Males						Females					
	Period			Percentage compared with 1921–30			Period			Percentage compared with 1921–30		
	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5
35—	16	46	69	100	288	431	4	12	16	100	300	400
40—	37	124	206	100	335	557	8	24	36	100	300	450
45—	75	282	466	100	376	621	16	53	86	100	331	538
50—	147	576	916	100	392	623	34	117	186	100	344	547
55—	266	963	1571	100	362	591	65	243	397	100	374	611
60—	439	1523	2380	100	347	542	136	510	771	100	375	567
65—	653	2247	3417	100	344	523	242	897	1446	100	371	598
70—	829	3067	4403	100	370	531	339	1338	2149	100	395	634
75+	913	3735	5582	100	409	611	437	1960	3019	100	449	691

being approximately ten years between the first and second epoch and approximately seven years between the second and third. Broadly speaking the statistical pattern for both sexes is similar. Between age 40 and 75 years there was an increment of approximately 250 per cent in the mortality in each of the intervening age groups in 1931–9 as compared with 1921–30. The increase continued and in 1941–5 ultimately amounted to approximately 450 per cent. The statistics also indicate that in middle age, 40–55 years, the male death-rate was increasing more rapidly than that for females, whereas in old age the position was reversed. Since, on the whole, there has been a fairly uniform increase in the mortality throughout life, the increment which has occurred in middle age being not very dissimilar from that for older people, it is extremely unlikely that transference of deaths from " old age " affords an adequate explanation of the increased mortality from coronary disease.

(ii) *Myocardial disease*. The relevant statistics for myocardial disease are stated in Table IV. Here again there is a close agreement in the statistical experience of the two sexes. Between age 40 and 65 the rates increased approximately 50 per cent for both males and females in 1931–9 as compared with those in the initial period; subsequently, they decreased, with the result that in 1940–5 the ultimate excess, except at age 75+, was of the order of 30 per cent for males and 20 per cent for females.

Transference of Myocardial Deaths

Attention has been previously drawn to the decline in the comparative mortality index, at age 35 years and upwards, for myocardial disease since 1941. It would appear from Table IV that each age was affected, as the death-rate in every age group in the period 1940–5 is lower than the corresponding value in 1931–9. This fact would seemingly indicate that some deaths previously certified as due to this cause are now ascribed to one or other of the forms of circulatory disease. The relevant questions then arise; is it possible:

(1) To estimate the extent of this transposition?
(2) To ascertain if the coronary disease mortality has been credited with the transfer?

The clinical features of coronary thrombosis were first clearly presented in England by McNee (1925). A lapse of fifteen years before the acceptance of a more precise classification of causes of cardiac deaths became general would not be remarkable. The following procedure was adopted to provide an answer for which no exact precision is claimed, but only a fair degree of approximation. It was assumed that the age-specific death-rates for both myocardial and coronary disease increased linearily during the period 1931–9, which means that the equation of a straight line describes their course during the years in question. The constants obtained from these linear equations for each age group were utilized to forecast the expected age-specific death-rates in 1945. Admittedly, extrapolates obtained from such limited experience, and for so relatively wide an interval of time, are not entirely satisfactory. Nevertheless, the procedure offers the only adequate method of approach. The comparison of the actual and predicted rates of mortality at ages (adjusted for change in classification) for each of the two causes of death is made

TABLE IV

THE DEATH-RATES PER MILLION OF POPULATION IN AGE GROUPS FOR MYOCARDIAL DISEASE IN ENGLAND AND WALES FOR CERTAIN EPOCHS

Myocardial Disease

Age group	Males						Females					
	Period			Percentage compared with 1921–30			Period			Percentage compared with 1921–30		
	1921–30	1931–9	1940–5	1921–30	1931–9	1940–45	1921–30	1931–9	1940–5	1921–30	1931–9	1940–5
35–	55	97	70	100	176	127	48	101	65	100	210	135
40–	116	214	152	100	185	131	91	184	122	100	202	134
45–	322	462	343	100	143	107	242	365	269	100	151	111
50–	628	1003	796	100	160	127	473	706	539	100	149	114
55–	1254	1932	1725	100	154	137	917	1376	1091	100	150	119
60–	2617	3935	3471	100	150	133	1928	2928	2371	100	152	123
65–	5392	7725	7027	100	143	131	3880	6008	5067	100	155	131
70–	10,213	15,904	13,922	100	156	136	7672	12,520	11,144	100	163	145
75+	23,777	40,988	39,153	100	172	165	20,508	36,382	35,099	100	177	171

in Table V. For coronary disease it will be seen that, for each age group, with one single exception (45–50 for males), the expected death-rate is greater than the actual death-rate. For males, apart from age 70+, the excess at the other ages is of the order of 10 per cent. For females the difference is somewhat greater. Hence it would appear that the mortality from coronary disease is now increasing less rapidly than in the period before the war. As was to be expected from the previous evidence, the gulf between the actual and predicted death-rates in 1945 for myocardial disease is not only much wider but, as will be noted, the disparity is correlated with age for both sexes. Up to age 55 the expected death-rate for males exceeds the actual by nearly 100 per cent. The difference subsequently declines and after age 60 it amounts to approximately 50 per cent. For females the difference is greatest at

TABLE V

THE ACTUAL AND EXPECTED DEATH-RATE PER MILLION OF POPULATION IN AGE GROUPS FROM CORONARY AND MYOCARDIAL DISEASE IN ENGLAND AND WALES IN 1945

Coronary Disease

Age group	Males		
	Actual death-rate	Expected death-rate	Difference as percentage of actual death-rate
45–	542	542	0
50–	1045	1168	−12
55–	1838	2008	−9
60–	2924	3140	−7
65–	4066	4313	−6
70–	5256	6126	−17
75+	6477	7723	−19
	Females		
45–	98	108	−10
50–	234	237	−1
55–	447	517	−16
60–	893	1039	−16
65–	1680	1850	−10
70–	2600	2787	−7
75+	3392	4390	−29

Myocardial Disease

Males		
Actual death-rate	Expected death-rate	Difference as percentage of actual death-rate
280	547	−95
659	1353	−105
1424	2666	−87
3065	5483	−79
6377	9424	−48
12,812	19,430	−52
36,250	54,681	−51
Females		
197	421	−114
461	838	−82
947	1524	−61
2097	3378	−61
4542	7024	−55
10,445	15,262	−46
33,517	47,289	−41

TABLE VI

THE ACTUAL AND "POTENTIAL" DEATHS PER MILLION OF POPULATION IN AGE GROUPS IN 1945 FROM CORONARY DISEASE ASSUMING THE MORTALITY HAS BEEN INCREASED BY TRANSFER FROM THE MYOCARDIAL GROUP

Age group	Potential death-rate = expected coronary death-rate plus difference between actual and expected myocardial death-rate			
	Males		Females	
	Actual death-rate	Potential death-rate	Actual death-rate	Potential death-rate
45–	542	542+ 267= 809	98	108+ 224= 332
50–	1045	1168+ 694= 1862	234	237+ 377= 614
55–	1838	2008+ 1242= 3250	447	517+ 577= 1094
60–	2924	3140+ 2418= 5558	893	1039+ 1282= 2321
65–	4066	4313+ 3047= 7360	1680	1850+ 2482= 4332
70–	5256	6126+ 6618=12,744	2600	2787+ 4817= 7604
75+	6477	7723+18,431=26,154	3392	4390+13,772=18,162

45–50 years—114 per cent—but no undue importance may be given to this value because the mortality at this particular age is low. At the other ages the decline approximates to that for the male sex, with the result that in old age the expected death-rate is roughly 45 per cent in excess of the actual.

Since the "calculated" age-specific death-rates from coronary disease in 1945 are greater than the actual, it would suggest either:

(1) that there has been little or no transference from the myocardial group to this category;

or

(2) that coronary disease in itself has decreased and that the high mortality now observable is actually due to a transfer of myocardial deaths.

Hence it is of interest to assess what would have been the position if the transposition had occurred. The most likely magnitude of the transfer would have been the excess of the expected over the actual death-rates from myocardial causes. The addition of this difference to the expected coronary death-rate would yield what we have called the "potential death-rate" from coronary disease in 1945. The result shown in Table VI indicates that if such a change or transfer occurred the coronary death-rate up to age 75 years for males would be doubled and, beyond that age, would be four times its existing size. The alteration in the female mortality would have been even greater.

Sex Ratio

Although the increment in the mortality from coronary disease has not been dissimilar for the two sexes, the dominance of the male mortality over that for females is excessive, as will be seen in Table VII which shows the male–female sex ratio at the various age groups and, in addition, similar

TABLE VII

SHOWING THE SEX RATIO $\left(\frac{M}{F}\right)$ AT AGE GROUPS FOR CORONARY AND MYOCARDIAL MORTALITY IN ENGLAND AND WALES AT DIFFERENT PERIODS

Age group	*Coronary Disease*			*Myocardial Disease*		
	1921–30	1931–9	1940–3	1921–30	1931–9	1940–3
35	4·0	3·8	4·3	1·15	0·96	1·08
40	4·6	5·2	5·7	1·27	1·16	1·25
45	4·7	5·3	5·4	1·33	1·27	1·28
50	4·3	4·9	4·9	1·33	1·42	1·48
55	4·1	4·0	4·0	1·37	1·40	1·58
60	3·2	3·0	3·1	1·36	1·34	1·46
65	2·7	2·5	2·4	1·39	1·29	1·39
70	2·4	2·3	2·0	1·33	1·27	1·25
75+	2·1	1·9	1·8	1·16	1·13	1·12

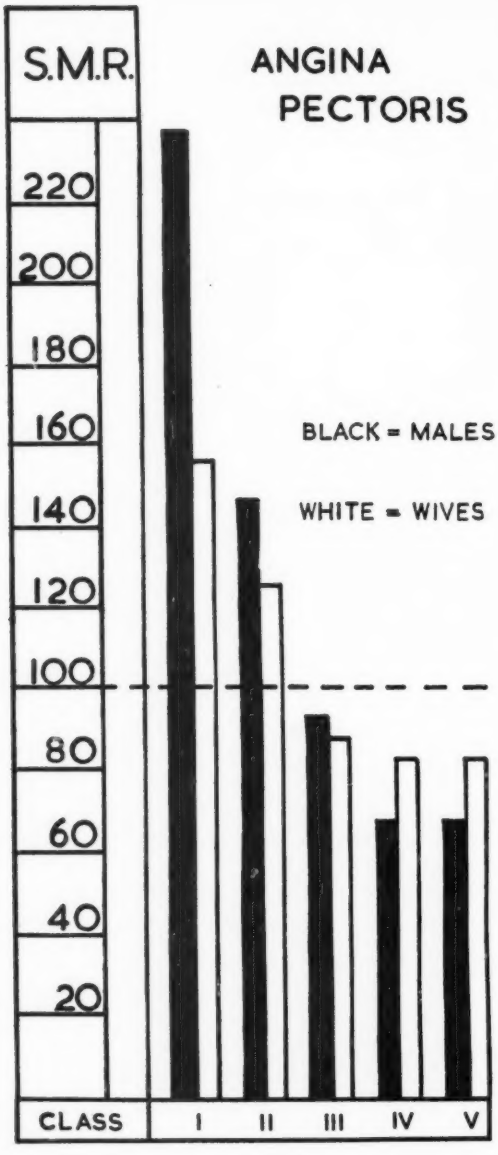

FIG. 3.—Standard mortality ratio from angina pectoris for men divided according to their social class as in the Registrar-General's reports, and for wives.

values for the myocardial diseases. For the latter, the male excess, after age 45, is of the order of 30 per cent, with no definite age association indicated in any of the three time periods. On the other hand, for coronary disease there is a decided relationship with age, observable in each of the three epochs. For example in 1940–5 the male death-rate at age 40–50 was more than 5 times greater than for females; at 55–60 the ratio drops to 4·0 and at 75+ it is less than 2.

This negative correlation of the sex ratio for coronary disease with age and the relative absence of any association in the case of myocardial disease suggests the impact of some factor detrimental to males in the causation of coronary disease. The most obvious sex discriminant is an occupational influence and, in this respect, the statistics available in the Registrar-General's Occupational Supplement for 1930–2 are instructive. In this very interesting and valuable report, the Registrar-General published the mortality from various diseases according to five social classes. The constitution of these social classes has so often been described that it is unnecessary at this stage to enlarge on their structure. It is sufficient to state that Class I is largely composed of professional workers, Class III represents skilled artisans and Class V unskilled workers—the two residual groups being intermediate to the contiguous grades. The correlation between the mortality from angina pectoris and social level is depicted in Fig. 3 in which it will be seen that, for both men and wives the decrease in mortality with descent in the social grading is clearly indicated. For males in Class I the mortality is 137 per cent in excess of the average for all males aged 20–65 years. It is 4 per cent in defect for skilled workers, and for unskilled workers the mortality is 33 per cent below the expected or normal value. If the occupations comprising the various social orders are studied separately the comparison is even more strikingly depicted, as will be seen from the mortality ratios in four occupations showing the highest and lowest values respectively (Table VIII).

These results clearly indicate the influence of type of work on the liability to death from coronary disease, since the four occupations having the highest ratios are those requiring not only a high degree of mental activity but also involve considerable anxiety and stress in their performance. For workers at the other end of the scale life is, from the point of view of mental activity, relatively less exacting and it would appear that their risk of dying from coronary disease is much more remote.

Realizing then that social or occupational status is a correlate of the mortality from coronary disease, it was of interest to ascertain if men and wives within

TABLE VIII

MALE OCCUPATIONS OF HIGHEST AND LOWEST MORTALITY FROM CORONARY DISEASE

Highest		Lowest	
	S.M.R.		S.M.R.
Physicians, surgeons	368	Coal miners below ground, engaged in other work	40
Proprietors of wholesale business	235	Stone miners and quarriers ..	38
Judges, barristers, solicitors ..	227	Agricultural and gardeners' labourers ..	32
Clergymen of Anglican Church	218	Workers in chemical processes ..	20

All males = 100.

(The standardized mortality ratio (S.M.R.) is the percentage ratio of the deaths actually registered in an occupation to those which would be expected to occur if the workers at age periods in that occupation experienced the age-specific death-rates for all males.)

the same social pattern were equally at risk. The sex ratios of their mortality in three age groups for angina pectoris and myocardial disease were evaluated and the results are stated in Table IX. For myocardial disease the variation in the size of the ratio, either according to social gradient or age, is of a slight order, whereas for angina pectoris the position is different; age is a factor, but social class more so. The importance of the latter is most obvious in the age period 45–55 in Social Class I, in which the male death-rate is almost ten times greater than that for wives; for skilled workers (Class III) the sex ratio is five; and it drops to 3 in the lowest social class. Why, it may be asked, is the ratio dominantly male in Social Class I at age 45–55? The most likely answer would seem to be that the workers included therein at this age period are those who have usually reached the peak of their professional careers and are exposed to the maximal strain associated with their particular responsibilities. Mentally, their tempo of life is fast and, as the sex ratio indicates, they are not "masters of their fate."

Cassidy, in his Harveian Oration (*loc. cit.*), asks the following question: "Is it possible that in the remarkable sex-incidence of coronary disease we may find some clue to ætiology? Can it be that masculinity predisposes one to coronary disease, and that feminity safeguards from it—that perhaps cholesteral metabolism is vitiated by maleness?" In this connection, it would seem important not to overlook the question of occupational influence and the fact that the mortality ratio of male professional workers to male manual workers is far higher than that of men to women.

Geographical Distribution

Finally, in this epidemiological survey it was of interest to depict the geographical distribution of the mortality from coronary disease throughout the country. A direct approach here is not possible because, although the Registrar-General has published, since 1940, the number of deaths from coronary disease in the several areas of the country, the age and sex composition of the population exposed to risk in these areas is unknown. In the present instance, an attempt was made to override this difficulty by comparing, for the twelve major geographical regions, the actual and the expected number of coronary deaths—the latter being estimated from proportional mortality ratios. The procedure of estimation was as follows. The proportion which the coronary deaths in age groups in England and Wales bear to the deaths from all causes at the corresponding ages was estimated for

TABLE IX

SHOWING THE SEX RATIO $\left(\frac{M}{F}\right)$ OF THE MORTALITY FROM ANGINA PECTORIS AND MYOCARDIAL DISEASE ACCORDING TO SOCIAL CLASS IN ENGLAND AND WALES IN 1930–2

Age group	*Angina Pectoris*			*Myocardial Disease*		
	Social Class			Social Class		
	I	III	V	I	III	V
45–55	9·9	5·3	3·3	2·2	1·3	1·4
55–65	4·6	3·4	2·4	1·9	1·3	1·2
65–70	5·0	2·4	2·2	1·9	1·4	1·4

the triennium 1941–3 and the results are shown in Table X.

TABLE X

RATIO OF CORONARY DEATHS PER 1000 TO THOSE FROM ALL CAUSES AT SPECIFIC AGE PERIODS

Age group. Years	Male	Female
—40	2·6	1·0
40—	35·0	9·1
45—	55·0	14·4
50—	71·5	21·8
55—	79·1	33·4
60—	78·4	41·2
65—	74·2	48·0
70—	70·0	41·3
75—	47·6	33·1
80+	29·0	20·6

These percentage ratios were accepted as " standard ratios " and applied to the All Causes deaths at the corresponding ages in each areal unit. On this basis the expected number of coronary deaths in each of the twelve major geographical regions of the country was obtained and then compared with the actual number of recorded coronary deaths in the three-year period 1941–3. Proportional mortality, which is the relationship of two variables, when used irrespective of age and time for comparative purpose, has recognized limitations. Possible allowance has been made for these factors in the present instance, but it is nevertheless advisable to test the validity of the adopted procedure.

There being no published statistics in areal units for coronary deaths prior to 1940 a test was made using nephritis as a criterion. The expected deaths from this disease for the two years 1931–2 were estimated in two ways:

(a) By the method of proportional mortality as previously described for coronary disease, allowance being made for the urban and rural character of the region.

(b) By indirect standardization, i.e. applying death-rates at ages from nephritis in the County Boroughs, Urban and Rural Districts in England and Wales to the populations exposed to risk in the specific areal or regional unit.

The expected number of deaths obtained on each of the two hypotheses were then related to those actually recorded. The test was made on the data for Warwickshire which contains the most populous County Borough—Birmingham—in England and Wales. The results are shown in Table XI. As will be noted the ratios obtained by the two different methods, are in very close accord. Hence it would seem that by using proportional mortality

TABLE XI

RATIO OF ACTUAL TO EXPECTED DEATHS FROM NEPHRITIS ESTIMATED IN TWO WAYS

	Birmingham		Warwickshire			
	C.B.		Urban		Rural	
	M.	F.	M.	F.	M.	F.
(a)	82	67	90	110	69	94
(b)	81	65	97	112	64	84

in the manner indicated, it is possible to estimate, with some degree of accuracy, the number of deaths from coronary disease that might be legitimately expected to occur in each of the twelve major divisions of the country.

The ratios of the actual and expected number of coronary deaths for males and females during the triennium 1941–3 have been worked out for these areas; both for males and females, there is a definite zoning of the mortality. Greater London has an excess of 21 per cent above the average or expected number for males; next in sequence is the group of residual South-Eastern Counties with an excess of 11 per cent, followed by North I where the actual deaths exceed the expected by 3 per cent. There is a large belt composed of North IV, Midlands I and II and Wales I in which the mortality is approximately 15 per cent below the average. The divergence between the results in Wales is noteworthy. In Wales I (South Wales) the recorded deaths are 15 per cent in defect of the expected number, whereas in Wales II (North Wales) the difference is one of 3 per cent.

The ratios for females are closely correlated with those for males, areas with high or low male mortality being also those in which the female deaths are also either in excess or defect of the expected value. The reason for these apparent geographical disparities in the size of the ratios is not readily apparent. Do they represent a true accounting or are they the resultant effect of differences in the social structure of the populations living in the different area units? It is not possible to give a definite answer owing to lack of appropriate data and it is obvious, from previous evidence, that social stratification is an influential factor in determining the mortality from coronary disease.

THE CLINICAL STUDY

General observations. The period covered in this part of the enquiry is approximately 23 years (1920–42), but the majority of the cases were seen

during a 15-year period (between 1925–39). The experience was that of a general medical consulting practice. The patients included in the series would thus represent, in the main, Social Classes I and II of the Registrar-General's classification by occupations, with a few from Social Class III. After excluding dubious cases the notes of 243 cases remained; these were primarily classified as *angina pectoris* (144 cases) or as *coronary thrombosis* (99 cases). Only 2 cases were accepted in which a history of characteristic pain was lacking. No cases of angina vasomotoria or of so-called " hypertensive failure " (Clifford Allbutt's " cardiac defeat ") were included, although high blood pressures must have added a load to hearts embarrassed by coronary disease in a number of cases. No cases were included of aortic valvular disease or aneurysm or of pernicious anæmia. This total of 243 cases of coronary disease represents approximately 1·7 per cent of all new private cases seen in consultation during this period. As no special reasons obtained for regarding the writer (J.A.R.) as a cardiologist, cases of heart disease should not have been referred for an opinion in any undue proportion. It is not known how the proportion would compare with that discoverable in family practices of varying type or locality.

Of the 243 cases in the series 164 were males and 79 females, giving an approximate ratio of M2 : F1. This corresponds closely with the sex ratio revealed by the All Ages Deaths from coronary disease in 1945. Cassidy (*loc. cit.*), in a more predominantly cardiological practice and in a much larger series of cases of coronary disease, records a ratio of M3·5 : F1. Of the 164 male cases, 97 (60%) were primarily classified as angina pectoris and 67 (40%) as coronary thrombosis. Of the 79 female cases, 47 (60%) were primarily classified as angina pectoris and 32 (40%) as coronary thrombosis. The relative incidence of effort angina and of coronary thrombosis was thus similar in the two sexes. On re-perusing the case-histories, however, it was found that angina pectoris (effort angina) had been preceded by an earlier account of a severe prolonged attack of pain, often lasting two hours or more (but without the more catastrophic picture of a severe coronary lesion) in an appreciable proportion of the cases. While most cases of effort angina probably start as such and may be assumed to be due to coronary sclerosis without occlusion, or even to coronary spasm (in association, commonly, with one or more of the general manifestations of hypertiesia), it would seem probable that small coronary occlusions (sclerotic or thrombotic), often unrecognized at the time, may not infrequently initiate the liability to effort angina.

In the 144 cases (both sexes), primarily classified as angina pectoris, there was a previous history of a prolonged attack of pain—not necessarily associated with effort—in 15 (10%). In 99 cases (both sexes), primarily classified as coronary thrombosis, there was a preceding history of effort angina in 28 (28%). Subsequent histories of the surviving cases of coronary thrombosis were not available in a sufficient number to allow of an estimate of the frequency with which this accident is followed by effort angina. It is well recognized that in some cases recovery is so far complete as to be followed by neither pain nor dyspnœa on exertion, sometimes for long periods. The above observations do little more than lend support to the common clinical and pathological opinion that effort angina and the status anginosus of coronary occlusion are expressions only of different stages or accidents in the same disease. They also suggest that the course and behaviour of the disease in the two sexes is similar, although its frequency is greater in men. It is clear that the two clinical syndromes, expressing coronary sclerosis and sclerotic or thrombotic occlusion respectively, can legitimately be discussed together in any consideration of epidemiology or of possible ætiological factors.

Age of Onset

Epidemiological studies of chronic types of disease based upon mortality figures are, as has been indicated, in a measure unsatisfactory in that they can give no account of the age of onset or of the occupation or other circumstances obtaining at the time of inception of the disease. The occupation recorded in a certificate is the last one preceding death. In 149 male cases and 69 female cases in this series it was possible to deduce, from the age of the patient noted at the time of the first examination and from the historical notes, the age *at onset* with a margin of error probably not exceeding one year.

TABLE XII

AGE OF ONSET OF CORONARY DISEASE

Age at onset:	Males (youngest) 34 (oldest) 90	Females (youngest) 35 (oldest) 83
	Age distribution at onset (males) in 149 *cases*	*Age distribution at onset (females) in* 69 *cases*
Under 36	2	1
36–40	2	0
41–45	12	1
46–50	23	7
51–55	21	5
56–60	23	12
61–65	28	19
Over 65	38	24

In 26 per cent of the male cases and 13 per cent of the female cases the age of onset was 50 years or less; in 74 per cent of the male and 87 per cent of the female cases the age of onset was over 50 years. The numbers are small but they suggest that the factors accounting for male preponderance are more operative in the earlier or middle than in the later period of adult life. This assumption is supported by the evidence that in England and Wales in 1946 the deaths from coronary disease amongst males aged 30–50 years constituted 6 per cent of the deaths from all causes in this age group, whereas the proportion for females was only 1·4 per cent. At age 50 years and upwards the corresponding values for males and females were 9 and 5 per cent respectively. Newman (1946) has reported on 50 young cases of coronary occlusion from the British armed forces which came under observation during the second world war. Of these, 39 were fatal (33 dying suddenly), and the diagnosis was established at necropsy. Coronary occlusion without thrombosis was recorded in 29 of the cases, and with thrombosis in 10. The youngest case was aged twenty and no less than 22 were within the age group 20–29. Of the 50 cases, 45 had been graded " fit " or " I " on joining the Service. There was only one female case in the series, but the ratio of men to women in the Services was in the neighbourhood of 10 or 15 : 1. A further reference to this group will be made in the section dealing with aetiology.

Occupation

In 100 male cases and 47 female cases at ages 65 or less the *profession or trade*, if any, was sufficiently clearly indicated to allow of an occupational classification. Of the women 11 were single and of these 5 were gainfully occupied. The married women were classified as " housewives "; four of them were, in addition, gainfully occupied.

TABLE XIII

OCCUPATIONS (males, aged 65 or less) (100 cases)

Business (including merchants, managers, stock exchange, shopkeepers, etc.)	39
Physicians and surgeons	19
Clergy	6
Officers (R.N., Army, R.A.F.)	6
Justices, judges, solicitors	6
Engineers	4

The remainder, each item of which scored less than a 4 per cent incidence, belonged to a great variety of professions and trades and included, for example, a peer of the realm; the driver of a hearse; a colonial rancher; a chief railway clerk; a professor of archæology; and the manager of a skating rink. Of males aged 50 or less at onset (total 39 cases), 12 (30%) were business men, and 11 (28%) physicians or surgeons. It has been previously indicated that according to the standardized mortality ratios published by the Registrar-General for the period 1930–2 the highest value was that for the medical profession (see Table VIII).

TABLE XIV

OCCUPATIONS (females, aged 65 or less) (47 cases)

Married women (classified as housewives)	32
Married women (engaged additionally in gainful occupations)	4
Single women (unoccupied or not stated)	6
Single women (gainfully occupied)	5

Special Stresses

In rather more than a third of all the cases (both sexes) there was a clear enough history of occupational, domestic or other stress preceding the onset of symptoms to warrant a consideration of these factors (in concert with the sex and occupational histories) as having a possible bearing upon ætiology. There was a record of " special stress " preceding the onset of symptoms (in most cases over a prolonged period) in 62 male cases and 27 female cases. Of those cases in which there was no record of special stress a considerable proportion were in retirement on account of age. The absence from the case-notes of a history of special stress in these and the remaining cases did not necessarily exclude its occurrence and in some cases the occupation alone made its operations probable. The occurrence of stress is thus under—rather than over—estimated. In a few cases sudden death or a coronary occlusion was shortly preceded by some grave strain or anxiety. Under the heading of special stress were included entries relating to mental overwork or worry in business or the home or in both; heavy public or other responsibilities; or other forms of sustained anxiety. In a few cases intimate knowledge of the patient's affairs was accepted as evidence of stress in the absence of a specific entry relating to it. As " the neurotic temperament " (in distinction from an ambitious or conscientious personality pattern) has sometimes been held to be an ætiological factor, entries bearing on this, or its combination with special stress, were also abstracted (Table XV).

Thus specific records of special stress occurred in at least 38 per cent of males and 34 per cent of females in the whole series. Of 9 (married and single) gainfully occupied women, all may be said to have been working under stress. The 5 occupied single women included: a nurse, still working to within 6 months of onset at the age of 62; the headmistress

TABLE XV

A. "Special stress"	*B. Neurotic temperament plus "special stress"*	*C. Neurotic temperament without record of "special stress"*	*No specific record*
MALES (164 cases)			
60 (37%)	2 (1%)	5 (3%)	97 (60%)
FEMALES (79 cases)			
22 (28%)	5 (6%)	1 (1%)	51 (65%)

of a big girls' school with many additional public duties and a history of severe mental shock preceding onset at the age of 51; a business woman, excessively nervous and conscientious, with onset at 62; a religious sister in charge of a large students' hostel, with a strong family history of coronary disease and onset at 50; and a massage and physiotherapy instructor, greatly overworked and with a high sense of duty, with onset at 46. If the male cases aged 50 and under at the time of onset are taken, there is a specific history of "special stress" in 21 (54%) out of 39 cases; 6 out of 9 female cases (married and single) aged 50 or under at onset (66%) gave a history of special stress. The occupations of the single women have been noted above. Of the duties of the modern housewife it may at least be said that her domestic responsibilities are seldom light, that her children, her husband and her home tend to be more seriously considered by her as the generations pass, that she often undertakes additional civic or social responsibilities and, in the social classes studied, commonly has a share in her husband's problems which was denied to the Victorian woman. After age 65 a high proportion of patients were in retirement; some of them were in their seventh or eighth decade; "special stress" would naturally, therefore, have become a less frequent entry. Reliable histories of stress in earlier life are not easily obtained from the elderly, but it was noted as having been operative at some stage in 10 cases (25%) out of 41 males, and in 5 cases (18%) out of 27 females in the later age groups (i.e. 65 or over).

It would be unwise to infer too much from the above figures. It is evident that stresses, both intellectual and emotional, must generally tend to accumulate towards the zenith of a career and to be fewer at its beginning or towards its close. It must also be allowed that, in the taking of clinical histories, modifiable conditions of life may be more carefully sought for in the case of younger and still occupied subjects. But neither of these considerations compels the exclusion of continuing or recurrent stress as an ætiological factor. The sex and occupational associations reviewed in the statistical study have already drawn attention to its probable importance.

Physical stress. In a few cases golf or tennis was continued into middle or later life, as an addition to an exacting professional career; a few patients had been athletes in their youth; one patient was a blacksmith. There was, however, no strong evidence to suggest that physical over-activity was a factor of comparable importance with mental or emotional over-activity. This is again in accordance with the conclusions to be drawn from the occupational incidence of coronary disease provided by the mortality data, which reveal the relatively low incidence of angina pectoris in manual workers as compared with the professions, to which attention has already been drawn.

Associated Illnesses

The association of angina pectoris and coronary thrombosis with gall-stones or cholecystitis has often been remarked. The incidence of clinically recognized gall-bladder disease in the general population within the age-period under consideration is not known, but it is doubtful whether it would be found to be as high as 9 per cent in males. On the general experience of hospital and private practice, peptic ulceration has a much higher frequency than gall-bladder disease. The incidence of duodenal and gastric ulcer in male factory populations and some other employments, according to Doll and Avery Jones (personal communication), is between 5 and 6 per cent. A figure of 6 per cent of cases of peptic ulcer in the males of this series is not necessarily, therefore, in excess of anticipation. Migraine has been stated to be common in the histories of anginal cases. The incidence recorded in this series is probably underestimated (a) because a history of it was not particularly sought for, and (b) because it would not, as a rule, be spontaneously mentioned by patients in a request for an account of

TABLE XVI

ASSOCIATED ILLNESSES

	Males (164)	*Females* (79)
Gallstones and cholecystitis	15 (9%)	6 (7%)
Duodenal ulcer	10 (6%)	Nil
(One case had a history of both duodenal ulcer and gall-stones; one of a duodenal and a gastric ulcer.)		
Other vascular lesions	7 (4%)	6 (7%)
Obesity	5 (3%)	7 (9%)
Migraine	5 (3%)	Nil
Diabetes or glycosuria	4 (2%)	4 (5%)

" previous illnesses." If there is more than a chance association between migraine and angina, it is probably related to the fact that the same temperament predisposes both to migraine and angina, that both are noted as commoner in professional workers, and both tend to run in families. The incidence of *obesity* has also been underestimated in this series, as only the more obvious cases received specific entry. Although weights were routinely recorded, except in bedridden cases, heights were not, so that height-weight ratios could not be determined. It is doubtful whether obesity is causally related to coronary disease, although it is well known that it may add an extra load to an already incommoded heart.

Other vascular disease. Cassidy (*loc. cit.*) found that hyperpiesis (e.g. a blood pressure of 160 systolic and 100 diastolic or more) was present in nearly 70 per cent of his cases lacking a coincident or recent history of coronary occlusion. In the 150 cases of this series, in which the notes included a clear record, blood pressures of 160/100 or over were recorded at some stage of the disease in 66 cases (44%); a further 7 cases (5%) gave systolic readings of 170 or over with diastolic figures below 100. Very high readings were frequently recorded in uncomplicated angina pectoris and low readings were by no means the rule after a coronary occlusion. If we accept angina pectoris and coronary occlusion as local manifestations of a more general arterial disease, it might be expected that vascular changes or accidents affecting other parts of the body (e.g. cerebral hæmorrhage or thrombosis, retinal hæmorrhage or peripheral arterio-sclerosis with intermittent claudication) would be a common association. In fact there was, up to the date of the last entry, a history of other local vascular symptoms preceding or succeeding the onset of coronary disease in only 7 male cases (4%) and 6 female cases (7%). The reasons for local selective actions in arteriosclerosis have yet to be explained. Normal blood pressures do not exclude its presence.

Taking the men and women together there was a record of syphilis in 3 cases, but none showed signs of cardio-aortic syphilis; of coincidental hyperthyroidism in one case; of hypochromic anæmia in 2 cases (one with a coronary thrombosis and the other with effort angina and a history of angina pectoris in four generations); of asthma in 2 cases; of gout in 2 cases; of paralysis agitans in one case; of diverticulitis in one case. There was one case with an earlier history of unilateral pyonephrosis and one of chronic Bright's disease. Four patients had a synchronous carcinoma of the stomach or bowel; one had had a malignant ovarian cyst removed.

Tobacco and Alcohol

Detailed records of the amount smoked were not kept. Although a large number of men were considerable smokers, in only 2 cases was there a note of " excessive " tobacco consumption; in 4 there was a record of alcoholism; and in 1 of an excessive use of both tobacco and alcohol. Although the majority of men with angina pectoris were smokers, non-smokers are certainly not immune. Among the women of the period and the age-groups reviewed smoking was rare.

Family History

Family histories, at no time easy to secure in accurate form, are inevitably defective for this further reason—that sympathetic consideration often compels the avoidance of detailed enquiries about cardiac illness and deaths in the parents or other near relatives of persons themselves the subjects of heart disease. The physician is also faced with the difficulty of deciding in the case of coronary disease, whether to include only cardiac cases or all instances of arteriosclerotic illness in the families studied.

Cassidy (*loc. cit.*) states that " family history played a part " in " almost exactly half his cases," but he supplies no details. For the reasons given, family histories were not consistently enquired into in this series; in the anxious situations accompanying a coronary occlusion they were often not asked for. There were, however, positive family histories of certain or probable coronary disease relating to a parent, a brother or sister, or others in the direct line in 12 male cases (7%) and in 8 female cases (10%). Among the males there was one instance of the same disease in a father and an uncle; one in a father and a brother; one in two brothers. The probable influence of heredity (whether operating through physical, mental, or temperamental predisposing factors or some combination of these) is supported by such histories as the following, which are taken from the present series:

(a) One medical man, who developed his symptoms before the age of 39, lost a brother from coronary thrombosis in his early thirties.

(b) One religious sister, who developed angina pectoris at 50, gave a history of cardiac deaths in her father, paternal grandfather and grandmother and a paternal great-grandmother and of others in these generations, usually between the ages of 50 and 60. Her mother's side of the family was healthy.

(c) An unoccupied spinster, developing symptoms at 60, gave a history of angina or cardiac deaths in her father, and her second and third brothers, and

of " strokes " in her fourth brother and her second, sixth and eighth sisters.

(d) Twin brothers (probably monozygotic twins), both formerly Army officers of high distinction and mental attainments, and having a remarkable identity of thought and taste, developed coronary disease within a few years of each other.

Of 20 cases (male and female) with positive family histories of angina, coronary thrombosis, or middle-age cardiac deaths, 13 (65%) developed symptoms at the age of 50 or less. In some other chronic diseases such as gout, due in part to an inherited factor, symptoms are apt to develop earlier in life where the family history is strong. Whatever the actual contribution of heredity to ætiology may be, the rising mortality from the disease and its occupational associations suggest that extraneous factors must be considered as of major importance.

Prognosis

A study of the natural history of a disease would be incomplete without a consideration of prognosis. A knowledge of social or group experience has interest in itself and value alike for life assurance and individual assessments. Unfortunately, reliable statistical studies of prognosis are at all times difficult and this is especially so in the more chronic types of illness. There are many circumstances that militate against careful follow-up enquiry in cardiac disease, whether in hospital or consulting practice. While it has always been recognized that angina pectoris is a condition in which precise forecasts, whether in respect of survival or of degrees and durations of improvement are scarcely possible, so many are the variable factors concerned, it would yet be of value if we could discover the mean expectation of life in relation to age of onset, mode of onset, and perhaps to some other factors such as ranges of blood-pressure or the presence or absence of other evidences of arterial disease. It is well known that one man may die in his first attack and that another may live for 20 years or more. John Hunter, notwithstanding that he continued to suffer frequent pain, lived and worked for 20 years after his coronary occlusion at the age of 41. Cassidy (*loc. cit.*) records two cases of patients surviving for more than 30 years, and one of a woman who died suddenly at 82, having experienced effort angina from the age of 30.

Where coronary thrombosis, as distinct from effort angina, is concerned there was a tendency to take too grave a view of prognosis following the recognition of the syndrome characteristic of the graver episodes which first became familiar in this country after the publication of McNee's paper (1925). While a coronary occlusion accompanied or shortly followed by congestive failure or arrhythmia is commonly succeeded by death in hours, days, weeks, months or at the most a few years, a study of bad attacks in respect of the severity and duration of the pain, but lacking these complications, may reveal a longer expectation of life, sometimes with a resumption of normal activities for considerable periods. With still slighter attacks the outlook may prove to be even better. From the present series three illustrative cases may be selected, each one clinically characteristic and confirmed by cardiographic and subsequent history.

(a) A surgeon, working under a very great physical, mental and emotional stress and a heavy smoker, developed effort angina at the age of 39. Some months later, at the age of 40, he had an extremely severe coronary thrombosis from which, for a time, it seemed almost impossible that he would recover. There were secondary complications in the form of an extensive pulmonary infarction with a pleural effusion and a prolonged phase of mental confusion. Within two years he was able to return to his hospital duties and thereafter continued them for a further 13 years, to the time of his death although always handicapped by an effort angina and latterly also by intermittent claudication.

(b) A general practitioner, after prolonged hard work and a sad bereavement, had an attack of coronary thrombosis at the age of 45. Three years previously he had had a cholecystectomy for gall-stones. He had otherwise been very healthy and a fine athlete in his youth. He retired from practice early, but was able to do a good deal of steady work in his garden and even for a time to play 36 holes of golf in a day. He remained liable to pain down both arms on walking after meals. He lived happily for 15 years and died during an afternoon nap in his garden.

(c) A masseuse and physiotherapist, the head of a large hospital department and a woman of great energy and with a high sense of duty, had a moderately severe coronary thrombosis at the age of 46. Subsequently she had symptoms of cholecystitis and at one time some gouty symptoms. She was still working in a private capacity 20 years after the original episode.

These three patients were all under 50 at the time of their first symptoms; all overworked; two were endowed with restless energy. About such younger cases, it may be reasonably argued that they lack the more widespread degenerative changes in the vascular system which develop in the later decades and that the coronary occlusion, in their case, is more in the nature of a local accident. As coronary occlusion commonly affects subsequent efficiency and the expectation of life in an adverse way, the interval that elapses between the first onset of effort

angina and a first coronary thrombosis or a prolonged attack of pain suggesting a small occlusion, might seem to have some bearing upon the prognosis of the uncomplicated condition. This interval could be estimated in 49 cases only. The approximate duration of uncomplicated angina of effort was estimated in 87 cases.

TABLE XVII

Interval between first onset of angina and first symptoms of coronary occlusion		Duration of history in surviving cases of angina uncomplicated by coronary occlusion (when last examined)	
Men and women (49 cases)		Men and women (82 cases)	
	cases		cases
Less than 5 years	43	Less than 5 years	69
More than 5 ,,	4	More than 5 ,,	4
More than 10 ,,	2	More than 10 ,,	8
		Twenty years ..	1

A physician is likely to see an undue proportion of cases in the earlier stages of the disease when they can be referred to him in his consulting room. As, furthermore, the numbers are small and a follow-up enquiry over a further 10 years or more might have been necessary in order to secure the final information in some cases, no conclusion can be drawn from this series with regard to the mean expectation of life at ages in cases of uncomplicated effort angina or of coronary thrombosis. Such conclusions could only be derived from collaborative morbidity studies undertaken by a number of general practitioners covering sufficiently representative social groups and areas of the country and over a sufficient period of time.

Case fatality. According to the data compiled by the Nuffield Bureau of Health and Sickness Records, Oxford, there were 196 patients with coronary disease admitted to the twenty-five hospitals within the Oxfordshire region during the three years 1945–47. The case fatality has been grouped according to age and sex and the All Ages fatality for men and women did not differ appreciably, being 61 and 66 per cent respectively. But at ages under 65 years the rate for males was much higher than that for females. Hence this small sample of hospital statistics, assuming it to be a microcosm of general outside experience, indicates that not only is the disease relatively more concentrated in middle-age in males than in females, but also that it is more fatal to them. It should be noted, however, that cases admitted to hospital are likely to include a high proportion of serious cases. There are, in fact, no means at present of ascertaining the case fatality at ages in the general community.

The above observations can only be held to indicate some broad probabilities in the disease as a whole in the groups studied.

Ætiology Reviewed

Where the predisposing and precipitating factors in a disease are several and there is no known specific agent of extraneous origin—a situation that obtains in many of the chronic endemic diseases of today (such as hyperpiesia and coronary disease, peptic ulcer, the chronic rheumatic diseases and the psychoneuroses)—and where, furthermore, the suspected factors must operate in varying combination and degree in different individuals, it is impossible, in the present state of our knowledge, to assess the full significance and relative importance of any one factor. In favour, however, of each of the five factors—familial predisposition, sex, ageing, certain types of professional employment, and mental and emotional stress—there is, as has been shown in the two main sections of this paper, considerable presumptive evidence. Furthermore, these factors often operate in conjunction:

(a) maleness on account of the occupations which it entails;

(b) the exacting character of sustained mental work accompanying intellectual occupations and posts involving heavy responsibilities;

(c) ageing, through mounting cares and the longer exposure to stress;

(d) the emotional tensions that frequently, on the one hand, accompany business, professional and intellectual life and interruptions to it, and, on the other, are expressions of

(e) the inheritance of an ambitious or conscientious personality pattern.

We have, at present, no reliable evidence bearing upon the association of special physical types. To the physician in his consulting room patients with angina pectoris present no such conformity of pattern as can be observed, for instance, in a high proportion of cases of duodenal ulcer. As in the case of hyperpietics, many anginal subjects are of good physique and have enjoyed excellent health in earlier life; this may have contributed to their energetic habits.

It may be argued, on the summary of the evidence presented, that the older the patient developing coronary disease the more have the ordinary exigencies of the years subscribed to the general and the coronary arterial degeneration; and that the younger the patient the more are we entitled to blame exceptional stress and the general pace and

fret of life in our modern mechanized world, in some cases with the added influence of familial predisposition. Statistical studies and clinical observations would seem, in the main, to support one another. Heberden's " disturbance of mind " is not to be ignored as a possible ætiological factor in coronary disease. The very fact that any of the more urgent emotions can precipitate anginal pain, and occasionally even a coronary occlusion, should suggest the possibility that repeated emotional disturbance or prolonged anxiety may have a continuing adverse influence on the coronary vessels. But, whatever part the stronger or more suppressed emotions may play, it would also seem, from the evidence here assembled, that sustained mental over-activity is another form of " disturbance of mind " which must be taken into account and considered as capable of affecting the coronary circulation and eventually of causing damage to the arteries and the heart. It is not possible to separate the effects of mental overwork and of the emotions (in the form of ordinary worries) which accompany it, but " the neurotic temperament " had a low incidence in the clinical series. Of all the extraneous factors inimical to hyperpietic subjects, with or without coronary disease, clinical experience, again and again, suggests that mental fatigue and strain and broken sleep are the most outstanding.

The possibility remains that business and the professions tend continually to select from the population those types of person who are most predisposed to the disease. This, however, would scarcely account for the steep rise in incidence and mortality within so short a period as a quarter of a century, and could only partially explain the occupational associations that have been demonstrated. Although it cannot be excluded it does not seem necessary to assume a contribution to male proclivity on the part of the sex hormones, nor is there any suggestion of sex-linked inheritance.

Of the *associated diseases* recorded in this series none would seem to be causally related, with the possible exception of gall-bladder disease. There would be no sufficient reason to think of a relationship in this instance on the score of its observed frequency, but for the further clinical observation than an acute cholecystitis sometimes closely precedes or succeeds a coronary thrombosis. This association should be worthy of more intimate study.

Tobacco. The fact that the majority of the women were non-smokers and that the disease can occur in male non-smokers, renders the influence of nicotine a doubtful one, although it cannot, as yet, be entirely excluded.

The Youthful Cases

Separate consideration must be given to cases in the youngest age-group (20–35). Through the kindness of the author of the paper relating to service cases, based on Ministry of Pensions records (Newman, *loc. cit.*), we have been provided with notes, not included in his account, bearing upon arm of the service, rank, duties and pre-service occupation for the whole group and abstracts of findings at necropsy in 28 cases. With the exception of one medical officer and two men promoted from the ranks during the war all were in the " other ranks " category. There was no indication in the brief records available that " special stress " had been a likely or, at any rate, a sustained experience during service or in civil life. Relatively few (15 out of 50) appear to have been on active combatant service. Most of the cases would have fallen into the Registrar-General's Social Classes IV or V. The ages of the 28 cases examined at necropsy varied from 20–35. In the majority of these arterial changes were so advanced as to suggest that the disease was of some standing and that it had probably started in civil life. The pathological descriptions were not characteristic of syphilitic arteritis. In 6 cases in the whole group the earlier civil occupation might have involved a lead hazard. Reading these records and finding few indications of special occupational stress or other extraneous factor, one might at first feel inclined to reconsider some of the conclusions drawn in the preceding sections. It must, however, be appreciated that these cases—even with the addition of others that may have escaped reporting—must represent a very insignificant proportion of the vast call-up for the three services during the war years. Coronary disease at or below 35 is, in fact, a very rare event. In 1946 the deaths from this cause in England and Wales under age 35 were 69 (0·37%) among 18,800 male deaths and 12 (0·12%) among 9,780 female deaths from coronary disease. Where extraneous factors in early life are far to seek it may possibly be shown that genetic influences play a more important part than habits of life and work.

Historical Retrospect

If the evidence here put forward, in the form of joint clinical and epidemiological studies, can be accepted as supporting the probable importance of an occupational type of hazard falling more heavily, and more considerably with the passage of time, upon those sections of the community whose work entails over-exertion of the mind rather than of the body, it would seem proper to enquire into the changing social circumstances and habits of our

present era and to compare present with past historical experience. It can scarcely be disputed (1) that the proportion of persons in the country who are professionally and intellectually employed has steadily risen since the industrial revolution of the nineteenth century in concert with such factors as increasing mechanization; the urbanization of the population (some 80 per cent of the people of England and Wales now live in urban areas as compared with 50 per cent a hundred years ago); and the extension of educational opportunity to all classes; (2) that the amount of mental work which can be accomplished by an individual in a day has considerably increased in the past century and especially in the last 25 years. The train, the motor car, the aeroplane; the telegraphic, and telephonic and ordinary and air-mail postal services; the competent secretary, the typewriter and the dictaphone—all these may have made the conduct of affairs more possible, but they have also multiplied the number of intellectual operations—all occasioning vascular responses—that can be performed within a given space of time. Competition in many spheres is more intense. Interruptions to concentrated mental work, which tend to give rise to irritation or frustration, also having their well known vascular accompaniments, are probably far more numerous than formerly. Refreshing sleep is more hardly won. Emotions are more consistently repressed than is the case among more primitive or rural peoples. Professional men a hundred years ago were often just as industrious, but the pace and tempo of their work and the knowledge and responsibilities required of them were of a different order. In no calling, perhaps, would the contrasts be found to be greater than in the medical profession which, of all occupations, shows the highest mortality from coronary disease.

Summary

In the review of the mortality from coronary disease during the past 25 years in England and Wales the following points of interest emerge.

The mortality amongst males and females aged 35 years and upwards in 1945 was 15 times greater than that in 1921 and the annual number of deaths from coronary disease is now approximately 25,000.*

The increments in the age specific death ratio rates for males and females were on the whole very similar, but there is evidence that in the age period 40–55 years the male death-rate was increasing more rapidly than that for females.

Although there was a fair degree of parallelism in the secular trend of the mortality from coronary and myocardial disease between 1921 and 1938, their subsequent statistical history differed, as the former has continued to increase whereas the latter declined. In 1945 the comparative mortality index for myocardial disease was 24 per cent in defect of the 1938 standard for males and 20 per cent for females.

The increase in the coronary disease mortality in the post-war period is unlikely to be wholly due to a transference of myocardial deaths because there is evidence that the coronary death-rate itself was increasing less rapidly in this period than in pre-war years—the actual death-rates at ages in 1945 being smaller than those predicted on the basis of the statistical experience relating to the period 1931–9.

There is evidence of a distinct sex ratio. The male death-rate in middle age is 5 times greater than that for females: subsequently the ratio decreases with increasing age and at age 75+ it is less than 2. There is no similar magnitude in sex differentiation for myocardial disease nor is there any definite correlation with age.

The most realistic explanation of this sex difference would be to ascribe it to an occupational or socio-economic influence. The mortality from coronary disease amongst men aged 45–55 in Social Class I is nearly 10 times greater than that of wives, and men of this social category are mainly those in professions and business administration, in which the mental stress and strain accruing from their responsibilities is heavy.

The mortality from coronary disease varies in different regions of the country. The significance and meaning of this geographical variation cannot be accurately assessed owing to absence of requisite information on the age and social stratification of the population within each areal unit. This knowledge is necessary because age and social status are important correlates of the mortality from the disease.

The mortality from cerebral vascular disease showed an increase parallel with that for coronary disease up to 1939.

The findings of the clinical study, making due allowance for its limitations, reveal a general conformity with those of the statistical study, and help to illustrate in a more detailed way some of the conclusions pertaining to possible causal influences. Age of onset has been discussed. It was 50 years or less in one-quarter of the men and one-eighth of the women. The need and some directives for further enquiry into prognosis have been indicated.

Disease of the coronary arteries has, finally, been considered briefly in its historical context and in particular relation to the remarkable social changes

* Deaths from angina pectoris and coronary disease in 1947 totalled 33,168.

that have occurred since it was first described 180 years ago.

Conclusions

The natural history of coronary disease has been discussed on the basis of a statistical study and of clinical experience, and in particular reference to its rising incidence and its social and occupational associations. The effect of multiple cumulative causes has never, perhaps, been sufficiently emphasized in considering the genesis whether of symptoms or of pathological changes. Effort angina induced by walking a given distance often occurs more readily (a) after a meal, (b) on a cold day, (c) in a state of anxiety or fatigue, than in the absence of one or more of these circumstances. Similarly, the buttressing effects of the several factors reviewed in this paper may be regarded as subscribing to the slow genesis of the underlying arterial change. There is nothing pointing to such alternative causal influences as infection or faulty nutrition. The chemical pressor substances that determine the vascular reactions are endogenous and the product of nervous stimulation.

Physicians are properly interested in the possible practical applications of their enquiries. It seems at present remotely unlikely that we shall discover a "cure" for general arteriosclerosis or coronary artery disease—some part of the processes involved being irreversible. In any case, diseases that attain a wide prevalence, having once been relatively rare, should be constantly considered with a view to a better understanding of how their incidence may be reduced—at least in those age-groups that cover the period of active work and citizenship. No such dramatic answers are here likely to be forthcoming as in the case of a bacterial or nutritional disease, but, even though they be counsels of perfection, we can at least argue that existing conditions of work in many professional and business careers impose strains which, when endured too long, are beyond physiological tolerance and that the conditions thus call for amendment; that members of predisposed families might sometimes be encouraged at an earlier stage, and even in the face of an activating conscience or ambition, to regulate their lives more rationally; that, in the field of personal hygiene, the organization of holidays, leisure, exercise and pleasurable relaxation is as sensible as attention to sanitary habits and balanced dietaries; and that the detection of hyperpiesia in the earlier phase by periodic health examinations could have value. The fact remains, however, that mental activity, unlike manual labour, cannot be readily limited by legislation or arrested by the clock. For some time to come we are, therefore, likely to witness a high toll of incapacitation and a sustained, perhaps increasing, death-rate from coronary artery disease affecting—and often at the time of their greatest efficiency—some of the more industrious members of the community in both sexes and in all classes, but more especially the male mental workers of the higher socio-economic grades. This trend is likely to continue—the general ageing of the population making its contribution—until such time as our social reorganization is directed in new ways and in better measure to the promotion of healthy living through a more precise physiological and psychological understanding of man and his capacities and a deeper appreciation of his individual and social needs.

References

Cassidy, M. (1946). *Harveian Oration. Lancet*, **2**, 587.
McNee, J. W. (1925). *Quart. J. Med.*, **19**, 44.
Newman, M. (1946). *Lancet*, **2**, 409.
Registrar-General's Statistical Reviews of England and Wales for the years 1921 to 1946. H.M.S.O.
Registrar-General's Decennial Supplement, England and Wales (1931), Part IIa. *Occupational Mortality*. H.M.S.O.

CONGENITAL AORTIC SEPTAL DEFECT

BY

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A defect in the wall of the ascending aorta leading to free communication with the adjacent pulmonary artery is a rare congenital abnormality. The opening in the anterior wall of the aorta is just above the semilunar cusps and leads directly into the pulmonary artery. Maude Abbott (1927) regarded it as a partial defect of the aortic septum, probably at the point where the distal bulbar swellings meet the aortic septum and above the junction of the aortic and interventricular septa. A commoner form of communication is between an aortic sinus and either the conus of the right ventricle (Abbott, 1919; Brown, 1939) or the right auricle (Goehring, 1920; Macleod, 1944), usually due to a ruptured congenital aneurysm of a sinus of Valsalva. Abbott (1937) also described a third rarer variety where a small hole in the aortic wall, just above the valves leads into the conus by an oblique channel. Here the aortic valves are usually bicuspid. An example of this type of abnormality was described by Rickards (1881).

This report concerns an example of the first of these anomalies, an example of value chiefly because there were no other congenital defects. The various features, clinical and pathological, to which the aortic septal patency had led, formed a combined picture of the pure defect that is rarely seen and therefore worth recording.

Case Report

A boy of 14 came under observation about two years before he died, when admitted to Horton Emergency Hospital in May 1943 for increasing dyspnœa on exertion and for palpitation. He had been breathless from infancy, and his activities had been severely curtailed since early childhood, though latterly he had done a light office job near his home. He had been prone to recurrent bronchitis and more recently to severe epistaxes.

He was a pale stunted youth with a kyphotic chest, the anterior wall of which bulged forward prominently on the left side. Cardiac pulsation was diffuse and thrusting, with the impulse maximal in the seventh space 16 cm. to the left of the midline. The beat was regular at a resting rate of 80 a minute. A diastolic thrill was easily palpable just inside the cardiac impulse and also to the left of the sternum at the base. A systolic and a diastolic murmur were heard all over the præcordia, the latter generally louder and more impressive and best heard in the pulmonary area and just internal to the impulse. The systolic element, loudest in the aortic area where it overshadowed the other, was well conducted to the root of the neck on each side. Both heart sounds were audible in all areas, and the pulmonary second sound was accentuated. The blood pressure was 130/40 and the pulse collapsing. Neither cyanosis nor clubbing were present, nor had he any congestive failure. Other systems were normal.

Radioscopy showed a huge aneurysmal shadow comprising the pulmonary artery and aorta astride the greatly enlarged heart (Fig. 1). The aortic component was normally sited but very pulsatile, and no separate aortic knuckle could be seen. In oblique views the ascending aorta was prominent, and a barium swallow showed a combined aorto-pulmonary impression. Both ventricles were very large, the right larger than the left, and the right auricle was also thought to be moderately enlarged. The left auricle was flat in the right (I) oblique position (Fig. 2), but the pulmonary artery radicles were all prominent and there was a marked hilar dance. Apart from their enlarged vessels the lung fields were normal. An electrocardiogram showed a rather low voltage R I, high R II and R III and a diphasic T I, but was otherwise unremarkable (Fig. 3).

After keeping fairly fit and at work until October 1944 he then began to have recurrent faints and increasing breathlessness, for which he was re-admitted the following January. He was still pale, but now moderately cyanosed as well, though he

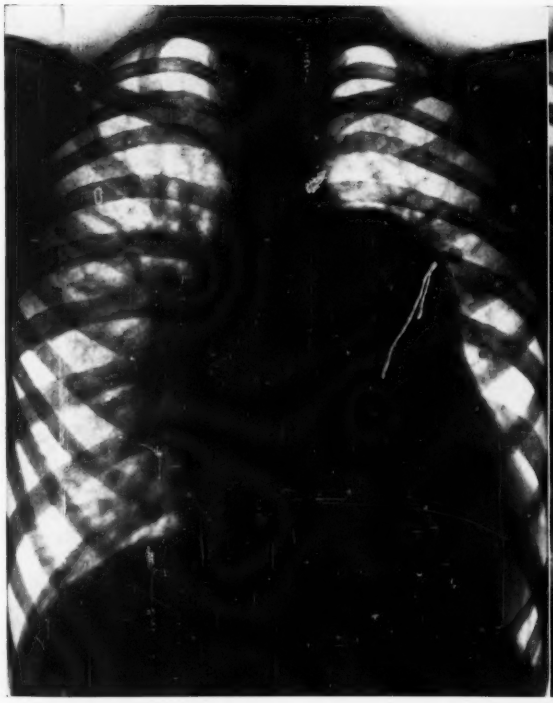

FIG. 1.—Radiograph (anterior view) showing aorto-pulmonary sac, enlarged pulmonary vessels and enlarged ventricles. 26/5/43.

FIG. 2.—Radiograph (right (I) oblique view) showing aorto-pulmonary sac and aortic arch above it, enlarged right ventricle and flat left auricle.

had a normal blood count. There was no congestion and his cardiovascular signs were unaltered except that the heart's action was more forceful and further enlargement of the aneurysmal sac and of both ventricles was evident radiologically (Fig. 4). He had repeated nose bleeds and also, from time to time, severe sweating attacks which were quite unexplained. There was no evidence of endocarditis or other infective process. He improved gradually with rest and was convalescent by March.

He was admitted for the last time seven months later in congestive heart failure. He had fallen ill a week before with catarrhal symptoms and was already in a grave state when admitted, orthopnœic, moderately cyanosed, and sweating profusely, though afebrile. The neck veins were much engorged, the liver enlarged, tender and pulsating, and there was dependent œdema. The left chest wall bulged even more than before and the action of the heart shook the whole thorax. The murmurs were unaltered except that the diastolic murmur was more obtrusive and now loudest in the mitral area. The

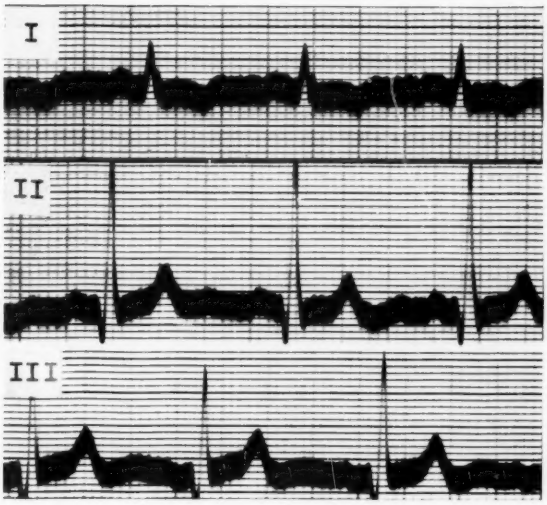

FIG. 3.—Electrocardiogram.

FIG. 4.—Radiograph (anterior view) showing further enlargement of aorto-pulmonary sac and heart, also more engorgement of lung vessels. 22/4/44. The maximum transverse diameter is now 18 cm. in a chest of 24·5 cm. instead of 16/23·5 cm. in 1943 (Fig. 1).

pulmonary second sound was very loud. Rest, sedatives, and diuretics failed to give relief and he died suddenly a few days later.

NECROPSY REPORT

The body was well nourished but undersized. Both lungs were congested and there was excess of straw-coloured fluid in the pleural sacs and about 350 ml. in the pericardium. The liver was enlarged and intensely congested.

In situ the heart was surmounted by a large aneurysmal sac comprising the main pulmonary artery and the contiguous aorta (Fig. 5). The heart weighed 390 g. and was greatly enlarged. Both ventricles were much hypertrophied and dilated, the right ventricle particularly. Their walls were of equal thickness, measuring 2·0 cm. across. In

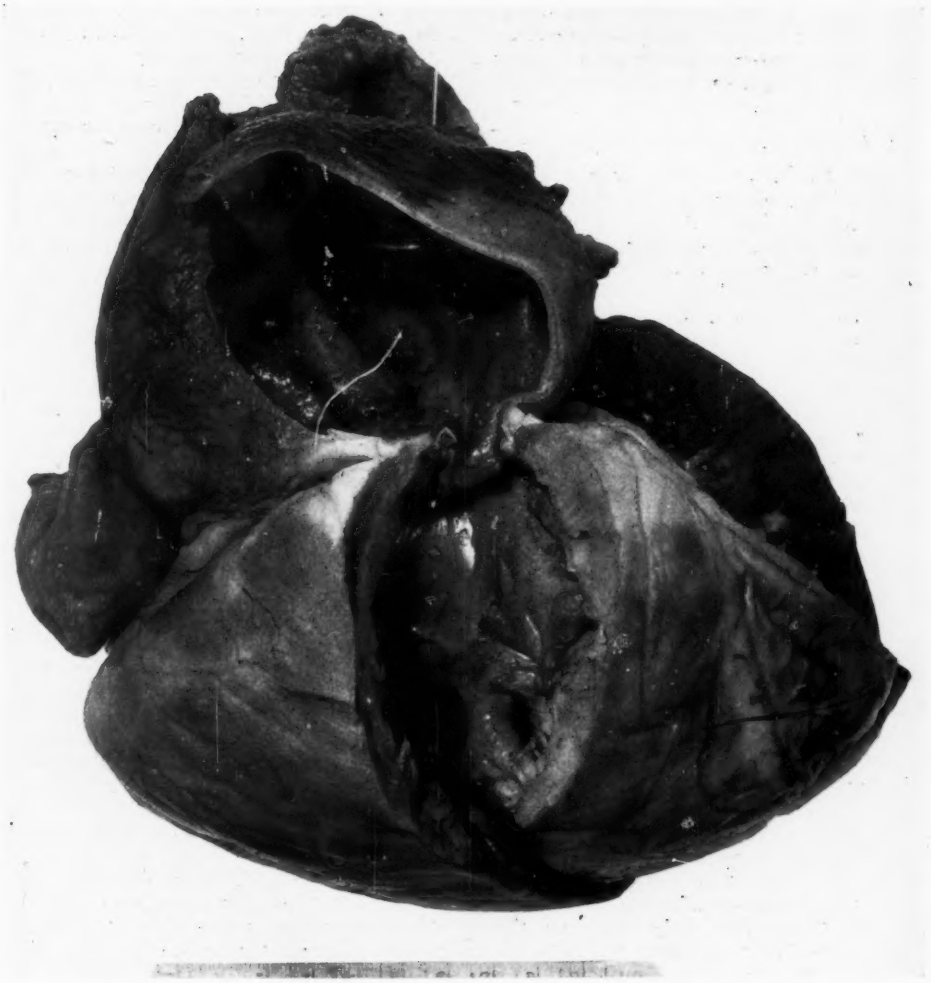

FIG. 5.—Necropsy specimen, anterior view, showing the aneurysmal sac.

contrast the auricles were not enlarged. All the heart valves were normal, but the mitral ring took three fingers easily. The interauricular and interventricular septa were normal.

The aneurysmal sac when opened showed a wide communication between the hugely dilated pulmonary artery and the base of the aorta, just above the valves. The defect measured 6·0 by 5·0 cm. Its edges were quite smooth, and a small septal ridge formed its lower border between the aortic and pulmonary valves. The valve cusps were all normally sited The size of the defect was such that it gave an appearance of both ventricles opening through their respective valves into a common sac from which the right and left pulmonary arteries arose above and posteriorly, and the aorta above, anteriorly and to the right. The aorta itself was markedly hypoplastic, measuring 4·1 cm. in circumference at the top of the arch. There was no coarctation; the innominate, left common carotid and left subclavian arteries were normally sited; and the fibrosed cord of the ductus was identified

above the aneurysmal sac. The main coronary vessels were normal in distribution and appearance.

Other organs were normal apart from congestion. Sections of the lung tissue showed no endarteritis.

Cases Previously Reported

Congenital aortic septal defects were reviewed by Hektoen in 1901, and by Abbott in 1927 and 1937. Hektoen had one case and collected nine others; one of these, mentioned already, was described by Rickards in 1881, and as it seems to belong to the rare third group of defect described by Abbott, we have not included it in this review. One further reported case was mentioned by Abbott in 1937, and Curtis Bain and Parkinson (1943) have since recorded another. The chief findings in these 11 cases are summarized in Table I.

The average age at death was 14 years, but this approximate figure is much affected by two of the series who survived to 37 (Girard, 1895) and 48 (Moorhead and Smith, 1922) years respectively, and in both of whom the septal defect was small. Three dying in early infancy (Gerhardt, 1874; Rauchfuss, 1878; Hektoen, 1901) are not fully described; and two (Baginsky, 1879; Cæsar, 1880) died respectively in childhood from convulsions during whooping cough and from brain abscess and tuberculous meningitis. Excluding all these, it is still evident, however, that the defect is a serious threat to life, for only one of the five remaining cases, including our own, survived beyond the second decade. Indeed, the most remarkable feature of our case was his survival until adolescence despite such a gross defect—a feature shared with the example reported by Bain and Parkinson (1943).

Though survival is variable, the physical limitations that the defect imposes appear to be almost uniform and always considerable. Symptoms of cardiac insufficiency from early infancy are always recorded where details are given, with one exception (Moorhead and Smith, 1922). This exception was a man of 48, fit until 9 months before his death when symptoms began suddenly with severe chest pain and dyspnœa. Although the sudden onset, rapid course and previous good health suggested an acquired condition, the absence of disease in the aortic wall compelled the authors to regard the defect as congenital. With the two exceptions already noted (Baginsky, 1879; Cæsar, 1880) and another three for whom the cause of death was not stated, all the others died with congestive heart failure. There is no record of endocarditis as a complication; and the only mention of clubbing is by Cæsar (1880) and Bain and Parkinson (1943) who noted its moderate degree. In both these clinical points there is a similarity to atrial septal defect (Bedford, Papp, and Parkinson, 1941).

The cardiac murmurs vary greatly. Cæsar (1880) specifically noted the absence of murmurs; and both Wilks (1859) and Girard (1895) mentioned only a loud systolic murmur over the base of the heart. Fräntzel (1868), Baginsky (1879), and Moorhead and Smith (1922) all described a double murmur. A loud apical diastolic murmur alone, with a thrill, was noted by Bain and Parkinson (1943). It is evident that basically the signs are similar to those of any other free leakage from the aorta above the cusps as with a patent ductus, a ruptured aneurysm of a sinus of Valsalva, and an acquired communication between the aorta and pulmonary artery. Abbott (1937) suggested that diastolic accentuation might be due to secondary pulmonary insufficiency. Although a functional incompetency may well have been present in our case, none could be demonstrated at necropsy. Abbott also noted that the double murmur seemed to be more superficial than that of a patent ductus, an observation that we can confirm. As in our case, Moorhead and Smith (1922) found a large pulse pressure; the only other record (Bain and Parkinson 1943) failed to show it.

The heart is always much enlarged. Dilatation and hypertrophy affect both ventricles, the right one especially. Aneurysmal dilatation of the pulmonary artery, by far the most impressive finding in our case, is by no means constant, a fact no doubt related to the frequency of small defects. Wilks (1859) drew attention, however, to the importance of pulmonary artery dilatation in his own case; and Bain and Parkinson (1943) found the pulmonary artery forming about two-thirds of the aneurysmal sac.

The site of the defect is remarkably constant and the lower border is formed by a smooth ridge of tissue separating the aortic and pulmonary sinuses. Though variable in size, the defect is generally small, about 1 cm. in diameter. In our own case it was 6 cm. × 5 cm., and, as in that of Bain and Parkinson (1943), was quite exceptional. The fine smooth edges are characteristic and distinguish the congenital from the commoner acquired communication between aorta and pulmonary artery (Brocq, 1885 and 1886). Moreover, acquired defects are accompanied by aortic disease, commonly a ruptured aneurysm of the ascending aorta (Porter, 1942).

Judging from the few records, other congenital cardiovascular defects are usually absent. Fräntzel (1868) found the pulmonary artery distributed to the left lung only, the right pulmonary artery springing from the ascending aorta. Hektoen's case (1901),

TABLE I.—Details of Reported Cases of Aortic Septal Defect

TABLE I.—Details of Reported Cases of Aortic Septal Defect

Author	Age	Sex	History and symptoms	Signs	Mode of death	Description of defect, heart and vessels	Ductus	Other defects
Elliotson (1830).	Young	F	Cyanosed from birth. Two weeks before death, œdema, cyanosis, orthopnœa.	Violent heart beat. No clinical disease of heart.	Congestive failure.	Opening at point where aorta and pulmonary artery lie in contact, admitting at least a finger.	Closed	None.
Wilks (1859).	8 mth.	F	From 4 months severe dyspnœa.	Loud systolic over base and greater part of chest.	Congestive failure.	Midway between valves and innominate artery: smooth edges, admitting goose quill. Rt. ventricle enlarged and pulmonary artery larger than aorta.	Closed.	Slight valvular patency of foramen ovale.
Frantzel (1868).	25 yr.	F	Dyspnœa and palpitation always.	Diastolic maximal at base to right of sternum. Systolic maximal at apex. Changing murmurs in two months before death.	Congestive failure.	1 cm. above aortic cusps, circular, 12 mm. in diameter. Left and right ventricles dilated and hypertrophied. Aorta larger than pulmonary artery.	Closed.	Pulmonary artery distributed to Lt. lung only. Rt. from ascending aorta.
Gerhardt (1874).	5 mth.	F	No details.	Harsh murmur over heart.	—	Just above valves, size of " half a lentil," sharp margins.	Not stated.	None.
Rauchfuss (1878).	Nursing.	—	No details.	No details.	—	No details, but stated to be similar to Gerhardt's specimen.	Closed.	No details.
Baginsky (1879).	4 yr.	F	From 8 days, repeated bronchitis and failure.	Many systolic and diastolic murmurs. Irregular rhythm.	Convulsions: pertussis.	Triangular, 0·5 cm. above aortic cusps, 1 cm. in largest diameter. Both ventricles hypertrophied; Rt. greater than Lt. Wt. 250 g.	Closed.	None.
Cæsar (1880)	9 yr.	M	Cyanosed from 8 months. Activity always limited.	No murmurs. Finger and toe clubbing from 3 months.	Brain abscess and tub. meningitis.	A little above aortic cusps, size of sixpence. Ascending aorta as big as an adult's.	Not stated.	Pulmonary valves perforated in several places.
Girard (1895)	37 yr.	M	From 1 year dyspnœa and cardiac distress.	Systolic murmur with accentuated second sound. Enlarged heart, gallop rhythm.	Congestive failure.	1 cm. above aortic cusps, 1 cm. in diameter. Hypertrophy, especially of Rt. ventricle. Aorta larger than pulmonary artery. Wt. 670 g.	Not stated.	None.
Hektoen (1901).	Newborn.	M	No details.	No details.	—	2 cm. above pulmonary cusps, oval, took tip of finger.	Patent.	Foramen ovale widely patent.
Moorhead and Smith (1922).	48 yr.	M	Sudden onset severe chest pain, dyspnœa, failing strength, last 9 months.	Double murmur, resembling aortic leak, to left of sternum. Diastolic conducted to apex. Large heart. B.P. 160 : 40.	Congestive failure.	2 cm. above pulmonary cusps, took tip of finger, opened into saccular dilatation of origin of aorta, which was stenosed above it.	Closed.	None.
Bain and Parkinson (1943).	18 yr.	M	Cyanosis and dyspnœa on exertion from infancy; worse for 6 years. Angina for 6 months.	Cyanosis. Moderate clubbing. Large heart, mainly to right with aneurysmal pulmonary artery. Apical diastolic thrill and murmur. B.P. 125/100.	Congestive failure. Sudden death.	Single aorto-pulmonary sac, 8 × 7 × 6 cm. Rt. ventricle greatly enlarged. Left ventricle normal.	Not stated.	Single brachio-cephalic trunk. Narrowed aortic orifice; funnelled orifices of both pulmonary arteries. Descending aorta arising from sac.

dying at birth, had a patent ductus and widely patent foramen ovale; and Wilks' case (1859) at eight months also had a slight valvular patency of the foramen ovale. Cæsar (1880) found the pulmonary valves perforated in several places. Bain and Parkinson (1943) found a common brachiocephalic trunk and funnelled openings from the sac into each main branch of the pulmonary artery. Apart from these few, the aortic septal defect has been the sole congenital abnormality in all the recorded examples. In contrast to this rarity of other defects, the communication produced by rupture of the right sinus of Valsalva into the conus is generally accompanied by a defect in the membranous part of the septum.

Diagnosis

The clinical recognition of congenital patency of the aortic septum is necessarily difficult, if only because of its rarity. In none of the recorded cases was the diagnosis made in life; and it is doubtful how far it has, in fact, been considered hitherto. Certainly in our own case it was not. We believed we were dealing with a complicated defect, including a patent ductus arteriosus and probably an atrial septal defect, a combined condition that has been reported and has been diagnosed during life.

The question remains whether a pure aortic septal defect can be recognized in life. Acquired defects are not uncommonly recognized (Porter, 1942; Schattenberg and Harris, 1943). Primarily the diagnosis depends upon signs of a free leak from the aorta in the presence of a dilated pulmonary arterial tree and enlargement of both ventricles. Such a combination is rare enough if we except patent ductus arteriosus either alone or along with an atrial septal defect. When a patent ductus is the sole abnormality, enlargement of the heart and of the pulmonary artery and its branches is rarely so striking as that found with the large aortic septal defects in Bain and Parkinson's case and in our own. As, however, the defect is often small, the same degree of enlargement is not always found.

The difference from a patent ductus would then be much less obvious, and a distinction have to rest with the more superficial murmur. When a patent ductus has anomalous signs, even no murmur, yet an unusually large pulmonary artery and branches, the difficulties in recognition may well be insuperable. The injection of contrast media by the basilic vein is unlikely to provide conclusive evidence regarding the exact site of the aorto-pulmonary leak because dilution in the pulmonary artery by the aortic blood would make radiographic interpretation so difficult. Perhaps in future retrograde angiocardiography may resolve the difficulty. It is said to outline a patent ductus very clearly, and would almost certainly show the site and size of an aortic septal defect.

Atrial septal defect alone, however, should be distinguishable, for here the auscultatory signs, though they may suggest an aortic leak, are not accompanied by excessive pulsation in the aorta and its main branches, nor by an increased pulse pressure. Moreover, dyspnœa is late as a sypmtom, so late that a fair capacity for exertion is retained even with an enlarged heart well into middle life, a further contrast with aortic septal defect. Also congestive failure is not found before the third decade of life, nor is the left ventricle characteristically involved in the cardiac enlargement. Atrial septal defects also give characteristic findings on right heart catheterization (Howart, McMichael, and Sharpey-Schafer, 1947).

If an atrial septal defect is accompanied by a patent ductus the similarity to a widely patent aortic septum is much more striking, especially in the degree of enlargement of right ventricle and pulmonary arteries. But here again catheterization might be expected to reveal the atrial defect and suggest this combination from the associated physical signs.

In so far as there is a common arterial sac with which both ventricles communicate, it might be expected that a persistent truncus arteriosus would most closely resemble a wide patency of the aortic septum; and yet, to judge from the records, this is not necessarily so. There is general agreement on the poor prognosis of a truncus, the presence of a systolic murmur and thrill along with much enlargement of both ventricles, and a broad vascular pedicle. But with a truncus, cyanosis is usually early and marked, although Taussig (1947) has recently claimed that this is the case only when the pulmonary circulation is maintained largely through the bronchial arteries The main pulmonary arteries are then either absent or rudimentary, and the radiological counterparts are the finding of small and ill-defined hilar shadows, a concave upper margin of the left border of the heart, and a hazy margin of the aortic arch due to the abnormally large superior bronchial arteries arising from it (Taussig, 1947). These points might clearly help to separate a truncus case of this type from a simple aortic septal defect, though in her recent book Taussig (1947) makes no reference to the latter.

We also have to consider in differential diagnosis joint aortic and pulmonary valvular disease, aneurysm of a sinus of Valsalva, and an acquired as distinct from a congenital aortic septal defect. None of these is likely to be traced to early child-

hood by the symptoms and they all have the marks of acquired disease—rheumatic, syphilitic, or bacterial. An acquired aortic septal defect has a sudden, even dramatic, onset and runs a rapid course, commonly as a complication of an existing aortic aneurysm or, more rarely, of bacterial endarteritis. Evidence of an infection is in each condition more important as a guide than the details of cardiac enlargement or the nature of any murmurs. Combined enlargement of right and left ventricles, pulmonary arteries, and aortic root may be present in all of them as well as in congenital aortic septal defect; and along with this a double basal murmur, increased pulsation in the aorta and its branches, and an increased pulse pressure. Separation from congenital aortic septal defect may be feasible only if the probability of an acquired lesion in a subject past youth is integrated with collateral evidence of an infective cause.

Summary

An example of congenital aortic septal defect is described together with radiological and necropsy findings.

Reported cases are reviewed and the diagnosis discussed.

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References

Abbott, M.E. (1919). *Contributions to Medical and Biological Research*, New York, **2**, 899.

—— (1927). *Osler and Macrae's Modern Medicine*, **4**, 710.

—— (1937). *Nelson's Loose Leaf Medicine*, **4**, 269.

Baginsky, B. (1879). *Berl. klin. Wschr.*, **16**, 439.

Bain, C. W. C., and Parkinson, J. (1943). *Brit. Heart J.*, **5**, 97.

Bedford, D. E., Papp, C., and Parkinson, J. (1941). *Ibid.*, **3**, 37.

Brocq, L. (1885). *Rev. de Méd.*, **5**, 1046.

—— (1886). *Ibid.*, **6**, 786.

Brown, J. W. (1939). *Congenital Heart Disease*, London.

Cæsar, J. (1880). *Lancet*, **2**, 768.

Elliotson, J. (1830–1831). *Ibid.*, **1**, 247.

Fräntzel, O. (1868). *Virchows Arch.*, **43**, 420.

Gerhardt, C. (1874). *Lehrbuch der Kinderkrankheiten*, **1**, 244.

Girard, E. (1895). *Zurich, Dissertation.*

Goehring, C. (1920). *J. med. Research*, **42**, 49.

Hektoen, L. (1901). *Amer. J. med. Sci.*, **121**, 163.

Howarth, S., McMichael, J., and Sharpey-Schafer, E. P. (1947). *Brit. Heart J.*, **9**, 292.

Macleod, A. (1944). *Ibid.*, **6**, 194.

Moorhead, T. G., and Smith, E. C. (1922). *Irish Journ. med. Sci., 5th Series*, **1**, 545.

Porter, W. B. (1942). *Amer. Heart J.*, **23**, 468.

Rauchfuss, C. (1878). *In Gerhardt, C., Handbuch der Kinderkrankheiten*, 4, footnote 61.

Rickards, E. (1881). *Brit. med. J.*, **2**, 71.

Schattenberg, H. J., and Harris, W. H. (1943). *Amer. Heart J.*, **25**, 512.

Taussig, H. B. (1947). *Congenital Malformations of the Heart*, New York.

Wilks, S. (1859–60). *Trans. Path. Soc., London*, **11**, 57.

THORACOSCOPY AS AN AID TO DIAGNOSIS IN CONGENITAL HEART DISEASE

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The advent of surgery in the treatment of congenital heart disease has meant that accuracy in the detailed diagnosis of the anatomy of the great vessels has become a matter of paramount importance instead of, as was formerly the case, an interesting mental exercise. Especially is this so when we are dealing with cyanotic heart disease, of which Fallot's tetralogy forms 70 per cent of cases. Anomalies additional to the classical four are not uncommon and may compel an exploratory thoracotomy before a decision can be made as to which side is the better surgical approach.

Blalock (1946, 1947, and 1948) advocates that the approach be made on the side of the innominate artery, and points out that if the aortic arch is right-sided, the innominate artery is located on the left side. There is, however, as he states, a wide variation in the arteries arising from the aorta, and in some cases all four arteries have arisen independently from the aortic arch, there being no innominate artery at all. In 1947 he suggested the more extensive use of visualisation of the heart and great vessels by the injection of radio-opaque substances, but even this method leaves unsolved many questions that can only be answered after the vessels have been examined by direct vision.

These difficulties were brought home to us in the recent case of a boy of 14 on whom we operated, with Fallot's tetralogy and a complete right-sided aorta. Following Blalock's suggestion that in such cases the innominate subclavian was more likely to be found in the left hemithorax, a left thoracotomy was performed. The aortic arch was found to be high in the mediastinum, with the subclavian coming directly from its upper medial aspect. There was a gap of about an inch between the aortic arch and the hypoplastic pulmonary artery, but it proved impossible to bridge this by the short available subclavian artery even though a maximal length had been freed and turned down.

After this disappointment it was decided to attempt another diagnostic investigation in future cases, namely thoracoscopy after the induction of pneumothorax. Apart from the advantage that it is not such a major procedure as thoracotomy one hoped that this would supply the answer to many questions that exercise the mind of the surgeon before operating, such as the calibre and condition of the vessel wall, the extent of coarctation, and the condition of the aorta beyond the constriction. Thoracoscopy can be done on the table as a preliminary to immediate operation, or it can be done some days previously.

The following cases illustrate the use of this technique, the limitations and possibilities of which are still being investigated.

Case 1. A puny but intelligent girl, aged 7, was deeply cyanosed with gross parrot-beaked clubbing of fingers and toes. Clinically she appeared to be a case of dextrocardia with Fallot's tetralogy. On X-ray examination there was a pulsating shadow projecting from the heart on its left side and behind it. This shadow was provisionally interpreted as an enlarged auricle, possibly due to patent interauricular septum. Angiocardiography indicated that the ascending and transverse portions of the aortic arch and about one inch of the descending aorta were on the right side. Barium swallow showed no notching of the œsophagus to suggest a vessel crossing behind (Williams, 1947).

A left-sided pneumothorax was induced with 300 ml. of air. The next day a thoracoscope (G.U. type 9 mm. diameter) was inserted in the 6th left interspace near the angle of the rib, the patient lying on her right side. The lung was lying on the mediastinum but could be pushed out of the way

with the thoracoscope to reveal a "pulsating tumour" behind; the tumour was pink, smooth, retropleural and its pulsations were expansile; it emerged from the mediastinum and descended alongside the spine to disappear behind the lung. It was in fact the aorta which had crossed over the spine from the right side. The subclavian artery was concealed by the lung as it lay on the mediastinum.

Case 2. A Msutu boy, aged 3, suffered from coarctation of the aorta. He had had four episodes of left ventricular failure with triple rhythm, an alternating pulse (10 mm. of mercury) and moist sounds in the lungs, but when admitted his general condition was fairly good and failure had cleared apart from some rales in the left lung. Both carotids were pulsating vigorously, and the apex beat was in the sixth left interspace in the anterior axillary line. The femoral pulses could not be felt. A systolic murmur was heard over the third left interspace just lateral to the sternum. The blood pressure was 110/90 in the left arm and 170/120 in the right. There was some retarded development of the buttocks and legs.

X-ray examination confirmed the enlargement of the left ventricle and showed a normal aortic knuckle, but also slight enlargement of the right ventricle. There was notching of the ribs on the right side though not on the left. The following suggestions were made to account for his right ventricular enlargement.

(*a*) A patent interventricular septum, but the murmur was atypical.

(*b*) A co-existing patent ductus arteriosus without the characteristic machinery murmur. In view of the child's age it was difficult to dismiss this possibility, which would imply that the coarctation was infantile in type with a wider area of stenosis than usual. This was supported by the absence of notching of the left ribs.

(*c*) The four previous attacks of left-sided heart failure had resulted in hypertrophy of the right ventricle. The pulmonary vascular X-ray shadows were noted to be heavy.

Induction of a pneumothorax followed by screening and, if necessary, thoracoscopy presented itself as the simplest means of deciding, and was performed on the left side with 500 ml. of air. Screening showed that the lung was partially collapsed and, with the child vertical, was falling away from the mediastinum. The aortic knuckle pulsated vigorously, but seemed to be cut short about the middle of the arch. Three days later a thoracoscope was inserted in the 4th left interspace between the scapular border and the spine, the patient lying on his right side. Because the lung overlay the mediastinum the patient was then turned on his left side, and the table tilted into a moderate counter-Trendelenburg position. The view now obtained through a right angle vision telescope had completely changed: the lung had fallen outwards, downwards and forwards, putting the pulmonary hilus on a slight stretch (Fig. 1). The aortic arch was well exposed as it emerged from under the thymus, and the descending aorta could be viewed from above for a considerable part of its length towards the diaphragm. A tight coarctation was identified involving the root of a very small subclavian artery and extending for about 1 cm. outwards. The descending aorta was pulsating less than the arch above the coarctation, and there was less discrepancy between the calibre of the aorta distal and proximal to the coarctation than had been expected. Several large upper intercostal vessels were seen, and also a large internal mammary artery. The vasa vasorum on the descending arch just distal to the constriction were dilated. A good view of the surface of the lung hilus was obtained. No ductus arteriosus was visible nor fold of pleura raised by a ligamentum arteriosum. The lung and descending aorta appeared normal. After withdrawing the telescope air was sucked out of the chest and the wound closed with a stitch. The child slept for six hours following this procedure but next day developed a consolidation of the middle lobe of the right lung, from which he made an uneventful recovery. However, at operation one month later he died after the chest was opened and before the coarctation was excised. The heart stopped beating and could not be made to contract again. Post-mortem the heart weighed 121 grams, showing marked hypertrophy of the left ventricle and, to a less degree, of the right ventricle. There was no patent ductus arteriosus. The coarctation was confirmed at the level of the root of the atresic subclavian artery. Microscopic examination showed extensive perivascular fibrosis of the myocardium and intimal plaques of calcium in the coronary arteries.

Case 3. A European boy, aged 7, suffered from Fallot's tetralogy. He had been blue since the age of one year and cyanosis was increased by exertion. He could not run at all fast, and after ambling for about 30 yards he would squat on his heels.

On examination the veins of the neck were engorged above the angle of Lewis. The fingers were clubbed and the nails were cyanosed as was the face, even when at rest in bed. Arterial pulsation was visible above the clavicles. The apex beat was within normal limits, but there was a heaving impulse over the præcordium. A systolic murmur was present over the whole præcordium, loudest over

the second left intercostal space. There was no enlargement of liver or spleen. Blood pressure 110/90 in both arms. The red cell count was 7,100,000. X-ray examination showed right ventricular enlargement with the aortic knuckle on the left. The pulmonary conus was visible but diminished on its under side. The pulmonary vascular shadows were slight, especially towards the lung periphery. There was right axis deviation.

A right pneumothorax was induced with 400 ml. of air and a thoracoscope (Coryllos-direct) was inserted into the first right intercostal space in the midclavicular line. The subclavian artery was well visualized and also a considerable number of collateral vessels. The subclavian appeared to be a large artery and raised a ridge on the mediastinal pleura. A large innominate vein was seen with a vein running from it to communicate with a large azygos. The pulmonary artery could not be identified because of numbers of small engorged veins just above the hilus of the lung and the azygos vein. Although the pulmonary vessels could not be seen their position was estimated approximately from the level of the hilar pleura. The aortic arch was viewed travelling towards the left and not descending on the right side. The appearance of the subclavian artery suggested that there would be no difficulty in performing the anastomosis and this was confirmed by immediate thoracotomy on the right side.

Case 4. A Zulu girl, aged 9, was admitted in congestive heart failure. No good history could be obtained and it was impossible to find out whether she had ever suffered from rheumatism or not. The veins of the neck were engorged and pulsating two inches above the angle of Lewis. She had œdema of both ankles and an enlarged liver, but was not unduly breathless when lying in bed, but stated she was breathless when on her feet. Blood pressure 104/60. Pulse regular 144. The apex beat was in the 5th space just outside the midclavicular line. The præcordium was bulging and a diffuse heaving impulse was visible, with an apical systolic thrill. There was a harsh systolic murmur loudest over the apex but audible over the whole præcordium. In the 2nd left interspace an inch outside the sternal margin, there was also a sound that at times seemed to fill the whole diastolic pause, but because of the tachycardia it was difficult to decide whether this was really a machinery murmur or a third closed sound. Phonocardiography did not help. After a week's treatment with digitalis she came out of failure but her pulse rate never came

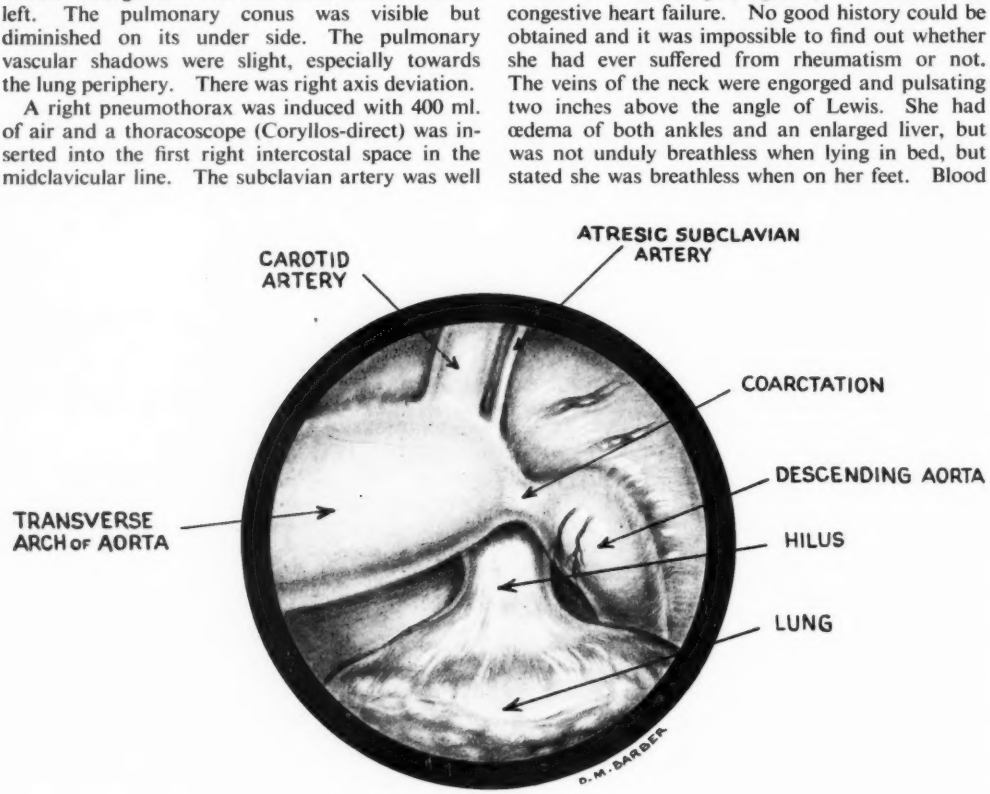

FIG. 1.—Case 2. Aortic arch seen from the side and above by right-angled telescope.

down below 120. X-ray examination and screening revealed a mitral-shaped heart, considerably increased in its transverse diameter. Both ventricles were enlarged, the right more than the left, and also the left auricle. The aorta appeared to be hypoplastic. There was some vascular congestion of both lung fields but no hilar dance. Various diagnoses were considered.

Cardiac catheterization (Dr. van Lingen) gave no evidence of an intracardiac vascular shunt. The catheter point failed to pass into the pulmonary valve and appeared to be washed back from it, which was regarded as evidence of pulmonary incompetence. However, in spite of the atypical X-ray and blood pressure we decided, in view of the child developed acute nephritis and operation has had to be deferred. Her heart rate is slower and the murmur is now typically machinery in character.

Case 5. A European boy, aged 9, was sent in as a case of coarctation of the aorta. The blood pressure in both arms was 150/120 and his femoral pulses could not be felt. His condition was complicated by petit mal. He was otherwise a bright and normal boy. It was decided to control the petit mal with phenobarbitone before operating and to perform thoracoscopy with the idea of not only viewing the coarctation but of assessing any change in the condition of the aorta that might occur subsequently.

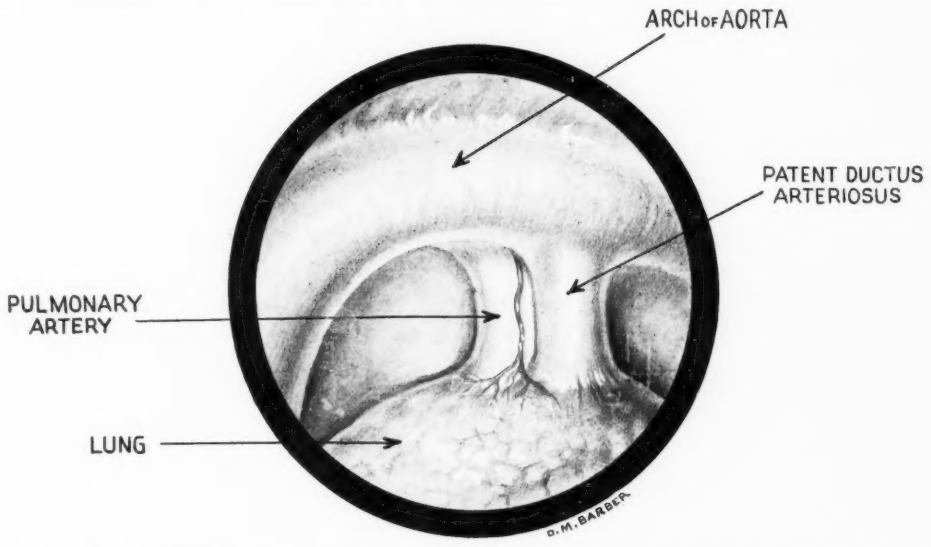

FIG. 2.—Case 4. View of aortic arch and lung root seen from above. Distorsion of the aortic arch is due to the proximal part to the left, being closer to the telescope than the other end.

very suggestive murmur, to attempt to exclude a patent ductus by means of thoracoscopy. Accordingly, a left pneumothorax was induced and a thoracoscope introduced by a posterior approach in the 4th left interspace close to the scapula with the child lying on her left side. This gave a good view of the hilus, and showed a large vessel underneath the aortic arch in close contact with it (Fig. 2). It was, however, difficult at the time to establish whether this was a patent ductus or the pulmonary artery. Its apparent origin from the anterior surface of the aortic arch strongly suggested a ductus, and in the light of further experience we are now convinced that this was so. Meanwhile the

A left pneumothorax was induced with 400 ml. of air and the thoracoscope was inserted immediately, using the anterior approach in the 2nd left interspace in the midclavicular line. An excellent view was obtained with the direct and also with the right-angled telescope. The coarctation was seen to be about a quarter of an inch long and slightly less in its outside diameter. The transverse aortic arch was dilated. Dilated subclavian and internal mammary arteries were clearly visible (Fig. 3). Unexpectedly a patent ductus arteriosus was seen arising close to the beginning of the coarctation, clearly separated from the pulmonary artery by a gap, and having a lymph gland overlying it. A small

vascular leash crossed over the ductus arteriosus. The vagus nerve, flanked by small arteries, hooked underneath and disappeared behind the hilus. The objective lens of the telescope could be brought into contact with the duct and its impulse with no thrill was easily felt on the shank of the thoracoscope. This manœuvre caused some discomfort to the patient. The ductus was wide and appeared to dilate aneurysmally with each pulsation. This patient is now awaiting operation, which seems imperative owing to risk of rupture of his aorta, the proximal part of which is very dilated. The ductus arteriosus will be ligated at the same time. At the moment he is undergoing treatment to control his epilepsy.

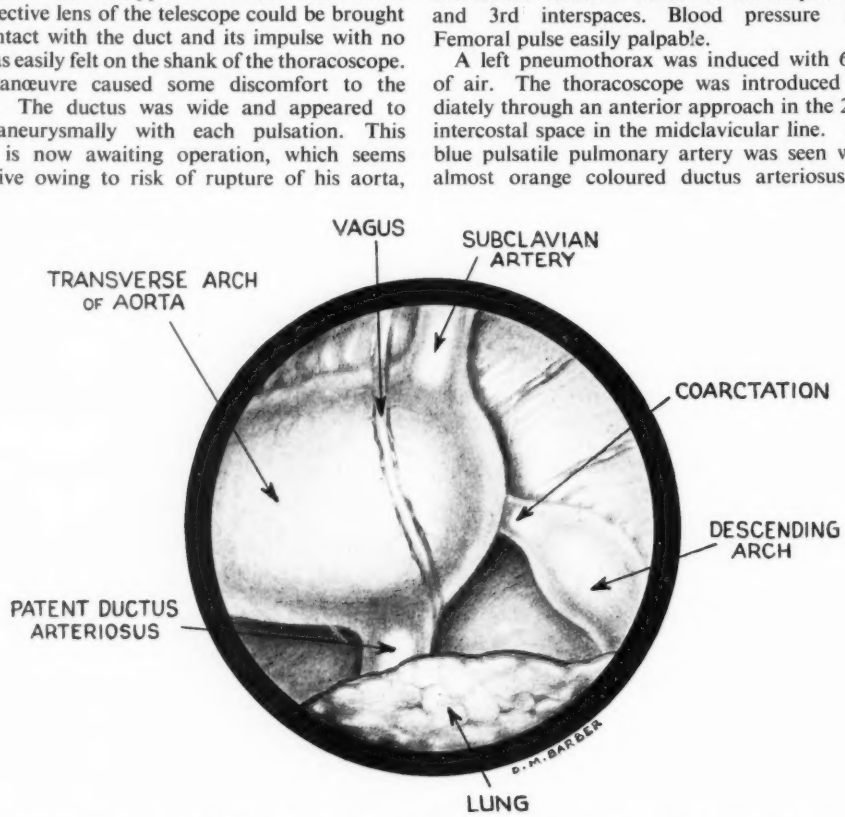

FIG. 3.—Case 5. The aortic arch seen from the front and above. The proximal aorta was greatly dilated and overlay the beginning of the coarctation. The vagus and its accompanying small vessels were more visible than usual.

Case 6. A woman, aged 21, noticed no symptoms as a child, but a " machinery murmur " was heard at the age of 9, and for this reason she was refused life assurance a few months ago. For the past three years she has been listless, tired, breathless on exercise, and dizzy on bending. She is due to get married shortly.

On examination, slight pulsation in the neck and second left intercostal space; no clinical cardiac enlargement; no thrill. A soft machinery murmur was heard in the 2nd left intercostal space, audible also at the vertebral border of left scapula in 2nd and 3rd interspaces. Blood pressure 150/60. Femoral pulse easily palpable.

A left pneumothorax was induced with 600 ml. of air. The thoracoscope was introduced immediately through an anterior approach in the 2nd left intercostal space in the midclavicular line. A very blue pulsatile pulmonary artery was seen with an almost orange coloured ductus arteriosus rising from the antero-inferior aspect of the aortic arch (Fig. 4). Pulsation of the ductus was less than that of the pulmonary artery. A small arterial leash was visible on the surface of the ductus with two small lymphatic glands along side. The aorta appeared to be somewhat angulated just proximal to the ductus but was otherwise normal. Operation performed on the following day confirmed these findings but, in addition, revealed a very slight indentation of the aorta just proximal to the ductus at the site where an infantile coarctation occurs. A very marked systolic thrill was palpable in the ascending arch up to the site of the constriction. By auscultation before and after ligation and

division of the ductus we both confirmed the disappearance of the murmur after ligation. Two days after operation it had returned, and this was confirmed when seen again one month later.

Case 7. A European male, aged 19, complained of slight blueness and dyspnœa, both aggravated by exercise, occasional slight giddiness on exercise, and some palpitation. His mother noted cyanosis at birth, aggravated by crying. He had been difficult to rear, but had suffered from the usual children's diseases, including whooping cough, without trouble. Walking was delayed until after the third year. No other members of the family suffered from congenital defects; his mother had been healthy during pregnancy and the labour had been normal.

Although early growth was retarded his height is 5 ft. 11 in. and weight 117 lb. His present activity is restricted to walking on the flat without hurrying. Cyanosis, which is minimal at rest, becomes pronounced on moderate exercise and during extremes of weather. Squatting is not marked, but he adopts a knee-chest position for comfort when fatigued. The parents think he has improved during recent years and are interested in the possibility of a Blalock-Taussig operation.

On examination, slight generalized cyanosis more marked in the lips, tip of nose, lobes of ears, fingers, and toes. Eyes suffused and marked clubbing of fingers. No venous engorgement in the neck. Blood pressure, right arm 125/60, left arm 115/60. No abnormality or evidence of congestion found in the lungs. Apex beat forcible and diffuse within the mid-clavicular line and in the 5th and 6th intercostal spaces. At the base of the heart there was a mild thrill with a loud systolic murmur in the second left space: this murmur was localized, but a softer systolic murmur was heard over the rest of the præcordium. The second sound was closed and much accentuated in the 2nd left intercostal space. Radioscopy showed some cardiac enlargement predominantly right ventricular, although the left ventricle was also enlarged to a lesser degree. The aorta pulsated vigorously. In the antero-posterior view the pulmonary conus was slightly prominent and not concave, but the left oblique view suggested that the pulmonary artery was small. Despite the prominence of the lung markings no pulsation was seen. A barium swallow showed the aorta to arch downwards on the left side. The X-ray evidence favoured Fallot's tetralogy with a good collateral circulation through a patent ductus or bronchial arteries; it did not suggest Eisenmenger's complex. Venous catheterization of the heart (Dr. van Lingen)

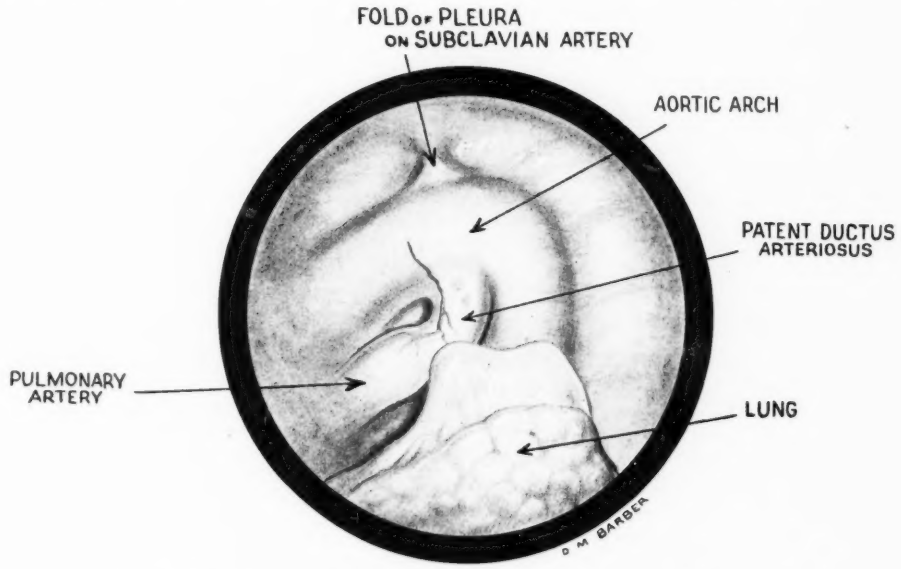

FIG. 4.—Case 6. Aortic arch and lung root seen from the front and above. The arch is more acutely angled than usual.

demonstrated the ventricular septal defect by passing the catheter through it, and analysis of blood samples suggested a right to left shunt. An overriding aorta was demonstrated with reasonable certainty by the fact that the oxygen content of the left ventricular blood was higher than that from femoral artery puncture. Failure to record pressures in the pulmonary artery or to obtain equal systolic pressures in the aorta and right ventricle precluded differentiation between Fallot's tetralogy and an Eisenmenger complex. The final diagnosis was Fallot's tetralogy with a possible patent ductus arteriosus or a collateral circulation to the lungs by bronchial arteries.

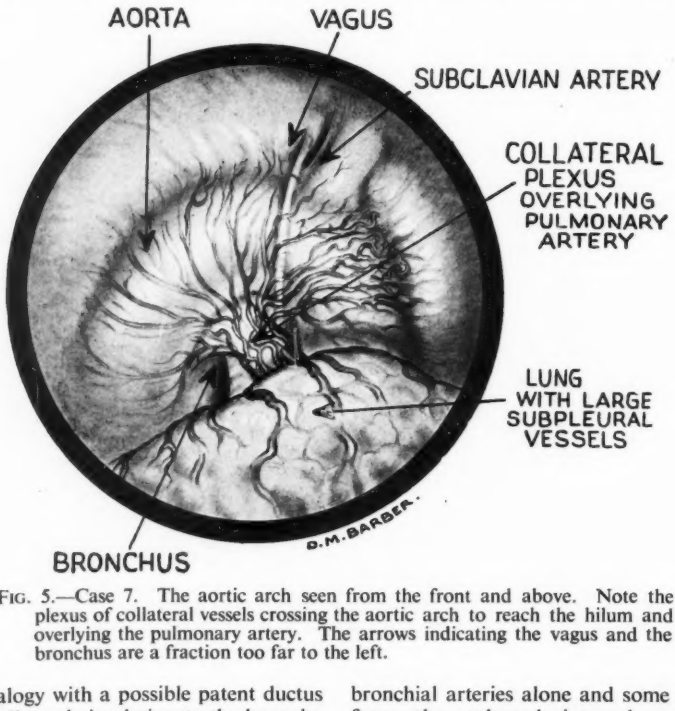

FIG. 5.—Case 7. The aortic arch seen from the front and above. Note the plexus of collateral vessels crossing the aortic arch to reach the hilum and overlying the pulmonary artery. The arrows indicating the vagus and the bronchus are a fraction too far to the left.

It was decided to submit this case to thoracoscopy in order to determine what form of collateral circulation was present and also, if possible, to take the pressure in the pulmonary artery by means of a needle introduced and withdrawn under direct thoracoscopic vision. A pneumothorax was introduced with 400 ml. of air, and the thoracoscope inserted in the 2nd left interspace in the midclavicular line, the patient reclining at an angle of 45° to the horizontal. The aortic arch was immediately seen, and presented a remarkable picture (Fig. 5) being crossed radially by numerous vessels, dark blue in colour and slightly tortuous, which entered the hilum as a network and almost hid the pulmonary artery. A few enlarged vessels were to be seen on the lung surface. In the angle between the subclavian artery and the curve of the arch another and thicker plexus of dark vessels was seen, presumably collaterals of the intercostal arteries dipping under the arch to enter the hilum. The vessels on the surface of the aortic arch numbered about 25, extending from the ascending aorta over to the descending, many more than would be expected from bronchial arteries alone and some seemed to come from the enlarged internal mammary artery. The pulmonary artery was small, and through another cannula, about an inch lateral to the first, a long needle was inserted into its small exposed part. The systolic pressure, read on a saline-citrate manometer, registered 20 cm. above the manubrium (normal 25 cm.). On removing the needle only a few drops of blood were seen and, when washed off with saline, did not reappear. Air was aspirated from the chest, the cannula removed and the wounds closed with one Michel's clip each. No untoward effects were noted by the patient, nor had any sensations been felt during the needling of the vessel.

The thoracoscopic finding confirmed that the collateral supply to the lung was good, though not provided by a ductus arteriosus. It also showed that, although the pulmonary artery was small, the extensive collaterals were enough to raise its pressure even at the hilum to four-fifths of the normal, and that it is easier to obtain the pulmonary arterial pressure by this method than by cardiac catheterization in cases of narrowing of the pulmonary infundibulum or valves.

On the reasonable assumption that a similar collateral supply was present on both sides of the aortic arch, it was thought wiser not to perform Blalock's operation on this patient.

Anæsthesia and Technique

In adults, local anæsthesia is the anæsthetic of choice, with omnopon, one-third of a grain, given an hour before. With suitable doses of omnopon the same anæsthesia applies to children down to the age of 7 or 8 years. Below this age, various types of general anæsthesia are used with equal success, and we have successfully given intravenous nembutal, or cyclopropane and oxygen after a basic narcotic of seconal, or ether by the closed method after a similar basal narcotic. Insufficient narcosis causes difficulty from restlessness and irregular movements of the chest, as the child is too unconscious to co-operate and not deep enough to be quiet. Even trilene anæsthesia is fairly satisfactory in spite of the rapid breathing if a large enough pneumothorax is induced. In children of five to eight years, 400 to 500 ml. of air can be introduced without distress.

The procedure of thoracoscopy need not be enlarged upon, as its technique is well known, but a few special points are worthy of mention. The pneumothorax is induced in the operating theatre, immediately before the operation, unless the lung is expected to be adherent, when the induction is done under an X-ray screen a day or two before. If there is widespread adhesion this method of investigation must of course be abandoned.

After trying various sites of introduction we have found the most satisfactory approach to be the anterior, in the second interspace in the midclavicular line, with the table tilted to an angle of about 45° in the counter-Trendelenburg position. A lateral tilt may be added, but is only occasionally necessary, if the greater part of the descending thoracic aorta is to be seen. For the visualization of a coarctation or of a patent ductus the direct telescope gives the best view; this should, however, be supplemented by the right-angled view, especially if the thymus or the internal mammary artery are to be seen. The subclavian artery in Fallot's tetralogy is better seen with a right-angled telescope but the direct telescope should also be available in order to obtain as good a three-dimensional idea as possible. When investigating coarctation, it is as well to insert the trocar and cannula as nearly as possible in the centre of the intercostal space to avoid both an enlarged intercostal artery and its anterior branch running along the upper border of the rib below; in practice, we have not met with this complication.

Any thoracoscope with direct and right-angled telescopes can be used; the 9-mm. Gullbring type as modified by the Genito-Urinary Co. has been very satisfactory; the 7-mm. Coryllos type gives a smaller field which is its only disadvantage. Oxygen can be given during the investigation, but is usually unnecessary even with cyanotic children, unless a very large collapse of the lung has been produced. The major operation can be proceeded with immediately, as was done in Case 3; no harm seems to have accrued from this, nor is it to be expected.

Discussion

We believe that thoracoscopy is a useful diagnostic procedure in certain congenital abnormalities of the great vessels and may give information that cannot be gained by X-ray examination even with the use of radio-opaque substances. The injection of these substances into the basilic vein often gives unsatisfactory results and when they are injected into the right auricle there is an appreciable risk to the patient's life, which is absent when the alternative procedure of thoracoscopy is employed.

As was only to be expected the hilar structures cannot always be visualized distinctly but, on the other hand, the gap to be bridged between the aortic arch and the pulmonary artery can be estimated fairly accurately. This was so in Case 3, where the pulmonary vessel was covered by a thick network of collateral veins and the artery could not be seen, though its position could be assessed with reasonable accuracy. In patent ductus arteriosus our experience indicates that an anterior approach gives a better view of the anatomy than a posterior and, while we would hesitate to claim that in cases in which no ductus can be seen its existence is excluded, we would emphasize that when a patent ductus is visualized it is unmistakeable.

In Case 4, the posterior approach was used and, although a structure was seen originating from the anterior aspect of the aortic arch, the limited field of vision made it impossible to be certain that we were not looking at the pulmonary artery itself. In the light of our later experiences with Cases 5 and 6 we now feel convinced that this was a patent ductus.

In childhood before the typical machinery murmur of patent ductus has developed, there seems to be

some value in thoracoscopy to differentiate it from other conditions, especially auricular septal defect. This difficulty was noted by Taussig (1947) who stated " in infancy there is nothing in this age group to differentiate this murmur from the systolic murmur associated with the patent ductus arteriosus or one caused by ventricular septal defect." There appears to be a place for thoracoscopy here. If the ductus is short it is more difficult to see than if it is long, and a " keyhole " ductus is almost certainly invisible.

The arch of the aorta can be viewed clearly and in coarctation the constriction can be seen and its extent estimated; one can also make sure that the calibre of the vessel distal to the coarctation is such that it can be anastomosed to the proximal segment. These items of information are difficult and usually impossible to obtain by X-ray methods and angiography. Crafoord (1945) reported two cases that were found inoperable at thoracotomy, and others have undoubtedly occurred.

Blalock (1946 and 1948) stipulates that a low pressure must be found in the pulmonary arteries before his operation is indicated. In doubtful cases in which a catheter cannot be passed through the pulmonary valve a thoracotomy is necessary to obtain this reading. As is demonstrated in Case 7 it may be possible to insert a needle into the pulmonary artery under view through the thoracoscope and thus obtain the pressure reading. This may not always be possible owing to anatomical variations but we claim that if thoracoscopy is practised as a routine investigation in these cases some thoracotomies may be obviated.

It is not always easy to diagnose the condition of double aortic arch or to differentiate the various types of anomaly involved. Sweet *et al.* (1947) describe a case in which the aortic arch was thought to be right sided, with a left-sided arch compressing the trachea; a left thoracotomy showed that the major arch was in fact left sided, but passed behind the œsophagus into the right thoracic cavity, where it was joined by a small right arch which produced the compression. A subsequent right thoracotomy enabled them to divide the right arch and effect a cure. Preliminary thoracoscopy in this type of case would enable a more accurate diagnosis to be made before operation, though here the procedure would have to be bilateral.

Conclusions

The technique of thoracoscopy as an aid to diagnosing certain congenital cardiac conditions has been discussed.

Seven cases are described in which this procedure was employed. The scope and limitations of this method have been briefly discussed.

We wish to thank Professor G. A. Elliott, Witwatersrand University, for permission to publish Case 7, and Dr. S. Selby, Coronation Hospital, for Case 2.

We are indebted to Dr. J. L. Lovibond for much helpful criticism, and to Miss D. M. Barber for the drawings.

References

Blalock, A., and Taussig, H. B. (1945). *J. Amer. med. Ass.*, **128**, 189.

— — (1946). *Bull. N.Y. Acad. Med.*, **20**, 2, 57.

—— (1946). *Ann. Surg.*, **124**, 879.

——, and Bahnson, H. T. (1948). *Annals Roy. Col. Surgeons of England*, **3**, 2, 57.

Crafoord, C., and Nylin, J. (1945). *J. Thorac. Surg.*, **14**, 347.

Sweet, R. H., Findlay, C. W., and Reyersbach, G. C. (1947). *J. Paed.*, **30**, 1.

Taussig, H. B. (1947). *Congenital Malformations of the Heart*. Oxford Univ. Press.

Williams, E. R. (1940). *Brit. J. Radiol.*, **18**, 323.

PROCEEDINGS OF THE BRITISH CARDIAC SOCIETY

The THIRTEENTH ANNUAL GENERAL MEETING was held at Newcastle, Co. Down, Northern Ireland, on Thursday, June 2, 1949.

Chairman: S. BOYD CAMBELL.

The Chairman took the Chair at 10 a.m.; 74 members and 17 visitors were present.

PRIVATE BUSINESS

1. The minutes of the last Annual Meeting, having been published in the Journal (**10**, 293, 1948), were taken as read and confirmed.
2. The balance sheet for 1948–49 was presented, having been audited and found correct by Bedford and Maurice Campbell. The credit balance on April 30, 1949, was £85 18*s.* 5*d.*
3. Lovibond and Bruce Perry were elected members of the Council in place of Brown and Cotton (terms of office expired).
4. Fraser and Hope Gosse were elected *Extra-Ordinary Members.*
5. The following Associate Members were elected as *Ordinary Members:*
   D. R. Cameron, W. J. Cooke, R. J. Duthie, Frances Gardner, G. W. Hayward.
6. The following new *Associate Members* were elected:
   J. Benn, Bristol
   W. W. Brigden, London
   T. H. Crozier, Belfast
   R. Daley, London
   Courtenay Evans, London
   C. J. Gavey, London
   G. A. Kiloh, Chester
   R. Kauntze, London
   A. Leatham, London
   J. W. Litchfield, London
   D. C. Muir, Hull
   D. A. Robertson, London
   A. J. Thomas, Cardiff
   B. G. Wells, London
7. The following *Associate Members* were elected for a further period of three years:

R. Kempthorne	C. G. Parsons
D. Lewes	W. K. Stewart
C. Papp	W. Stokes

8. The following alteration was made in Rule 22: " The subscription shall be fixed by the Council and shall not exceed two pounds a year for Ordinary Members and one pound for Associate Members; it shall become payable on the 1st day of March. Failure to pay the subscription due within two years shall be considered equivalent to resignation."
9. It was decided that an Autumn Meeting should be held in 1949 and that the Council should determine the date and the place of the meeting.
10. A memorandum by the Honorary Secretary on the International Council of Cardiology was considered. It was agreed that it should be left to the Council of the Cardiac Society to nominate a delegate and a deputy to the projected meeting of delegates to be held in Paris in 1950. It was agreed, at the suggestion of Bain, that there should be adequate representation of the British Commonwealth at the meeting of delegates.
11. A recent meeting of delegates to form a European Society of Cardiology was reported and some observations on this were made by the delegate of the British Cardiac Society, Evan Bedford. At the suggestion of Chamberlain, the Council was asked to consider whether or not the German Cardiac Society should be allowed to join the European Society of Cardiology.

DISCUSSION ON RHEUMATIC HEART DISEASE

Opening speakers:

(i) Ætiology of Rheumatism
   (*a*) Public health: A. C. Stevenson.
   (*b*) Pathology: J. H. Biggart.

(ii) Rheumatic Heart in Pregnancy
   (*a*) Clinical aspects: Robert Marshall.
   (*b*) Pathology: Florence McKeown.

A. C. STEVENSON (*introduced*). There is need for further illumination of the epidemiology of rheumatic fever; at times too sweeping deductions are made from the rather scanty data referring to juvenile rheumatism and its sequalæ. Certain limits can not safely be passed in interpreting the mortality figures of the Registrar General relating to acute rheumatic fever and heart disease. Moreover, little information is available from the School Medical Service and from notifications, and planned enquiries pursued over a long period from rheumatism clinics seem likely to be the most fruitful

source of information. Some figures are available relating to patients attending the clinic at the Royal Belfast Hospital for Sick Children.

Hypotheses concerning the relationship of streptococcal infections to juvenile rheumatism are based on scanty data. The conception of rheumatic fever as the end stage of a post-streptococcal state is interesting and attractive but does not appear to be based on much recorded observation. The evidence of familial susceptibility, as advanced most convincingly in recent years by Dr. May Wilson, of Cornell, has not received sufficient attention and even if the proposition of hereditary transmission of susceptibility by a single autosomal recessive gene is difficult to support, there is overwhelming evidence of some inherited susceptibility.

J. H. BIGGART (*introduced*). In spite of much research, the ætiology of rheumatic fever remains undiscovered. Theories involve the streptococcus pyogenes, streptococcus viridans, a specific streptococcus, or viruses, but the evidence necessary to establish any one of these is still lacking. The work of the German School has produced the theory of an allergic mechanism as the responsible factor.

Difficulties arise in accepting such an allergic hypothesis—the granulomatous character of the essential lesion, the limitations of its distribution to the cardiovascular system, the specific sites for its occurrence, and its specific life-history. In addition to such purely morphological reasons for challenging the allergic hypothesis, there is the clinical suggestion of the importance of upper respiratory infection as a precursor of the rheumatic attack.

Study of the lesions produced in the rabbit by serum hypersensitivity shows that many of these difficulties can be overcome. The granulomatous lesion, the specific distribution, etc., are duplicated in the experimental animal. It is therefore suggested that no matter what the ætiological agent of rheumatic fever it produces the specific histological picture through an allergic mechanism.

ROBERT MARSHALL (*introduced*). In spite of the steady fall in maternal mortality during the past 15 years, heart disease was actually gaining a more prominent position as a cause of maternal deaths. During the quinquennium 1943–47, 743 women in England, Wales, Scotland, and Northern Ireland have died from heart diseases associated with pregnancy and childbirth. The commonest lesion was mitral stenosis, a fact borne out by the figures collected by Kenneth Hudson from the Royal Maternity Hospital, Belfast, where in the years 1937–48 there were 24,078 total admissions, with an incidence of 1·8 per cent of heart disease, and a maternal death rate from this cause of 5·8 per cent; this compares with MacRae's findings in Queen Charlotte's Hospital, where the incidence was 0·8 per cent and the maternal death rate 3·1 per cent among 29,713 admissions. In Belfast 76 per cent of the deaths were emergency admissions, and 50 per cent occurred in connection with the patients' first pregnancy. These figures are comparable with those of Bramwell and Longson in Manchester, Carr and Hamilton in Boston, and Watson in New York.

The ætiological factor was rheumatic fever in 40 per cent of cases, and chorea in 12 per cent. A history of " ambulatory " pains was given in 15 per cent, but 22 had no history of relative disease. Mitral stenosis was diagnosed in 85 per cent of cases. It is of great importance to search carefully for this lesion during the ante-natal examinations, in order to eliminate admission to hospital of patients as " emergencies " with a high risk of death. As MacRae has stated, changes in the heart and circulation in pregnancy may cause breathlessness and palpitation, even in healthy patients; thus the cardinal signs of early congestive failure are rendered the more difficult to assess. Perhaps the most useful clinical hint is given by determining what number of pillows the patient requires at night. If signs of congestive failure are suspected during pregnancy, the patient should be admitted to hospital for a period of rest and observation, and all heart cases should be admitted at least a week before the date of expected confinement. While Caesarean section might still be advisable for cardiac, as well as obstetric, reasons, the practice of induction of labour for cardiological reasons has fallen into disrepute among obstetricians.

A series of 150 hospital in-patients during the years 1942–1946 has been reviewed. Of these, 8 are known to have died, and 36 have not yet been traced for various reasons. Of the first 100 patients reviewed, the ætiological factors and cardiac lesions corresponded closely with the larger series. Forty patients had been aware of cardiac symptoms during their first pregnancy, but 34 had developed such symptoms during their first pregnancy. Of these, 20 had suffered from rheumatism or chorea, but 14 had had no reason to fear heart disease, which was an additional argument for careful search for evidence of mitral stenosis at all ante-natal examinations. Five women had expressed the opinion that their health was better than before their confinements, 42 were thought to be unchanged, but 53 considered that their health had been impaired by pregnancy and parturition. It has to be remembered that it is not enough to nurse one's patient with mitral stenosis until her baby is safely

born, but that child-bearing is a prelude and a part of child-rearing.

FLORENCE MCKEOWN (*introduced*). A post-mortem analysis is presented of 9 cases of rheumatic heart disease complicating pregnancy. In 3 of these the strain of pregnancy was the apparent cause of decompensation. The mechanism of heart failure in these cases is debatable, but stress must be laid on the lesions of the coronary arteries which result from previous attacks of rheumatic carditis and appear to play an important part in lowering the cardiac reserve.

In the remaining 6 cases a recrudescence of rheumatic fever, which was usually sub-clinical, was responsible for decompensation. Sub-clinical rheumatism is of importance in relation to pregnancy, but only by routine post-mortem examinations, which should include histological study of many blocks of the heart, can the occurrence of such attacks be recognized.

The opening papers were followed by a discussion to which contributions were made by Bramwell, East, Gilchrist, Schlesinger, Bain, Abrahamson, and Crozier.

SHORT COMMUNICATIONS

VENTRICULAR SEPTAL DEFECT IN EARLY CHILDHOOD

BY A. RAE GILCHRIST AND ROBERT MARQUIS (*introduced*)

Although an isolated defect of the ventricular septum is recognized as one of the less serious congenital malformations of the heart, autopsy reports suggest that such a lesion is more frequently responsible for death in early childhood than is generally appreciated. Of Maude Abbott's 50 cases, 21 died at five years of age or under. In 110 consecutive cases of congenital heart disease coming to autopsy at under three years of age in the Edinburgh Royal Hospital for Sick Children, a defect of the ventricular septum, without other gross malformation of the heart, was found in approximately 25 per cent. In this group the predominant cause of death was an associated respiratory infection, but in a small proportion the death was primarily due to heart failure.

It is suggested that the differential diagnosis of congenital heart disease in young children must include the isolated ventricular septal defect, even when the disability is gross. In support of this contention 4 cases are presented. They conform to a general pattern of which the principal features are under-development from an early age, an absence of cyanosis, a liability to respiratory infections, and a tendency to congestive heart failure. The heart is enlarged, a loud systolic murmur is maximal up the left sternal margin, and the pulmonary second sound is accentuated. The electrocardiographic tracings are bizarre but suggest hypertrophy of both right and left ventricles. Radiological examination confirms this enlargement and shows the pulmonary artery to be enlarged and the hilar shadows to be prominent.

Autopsy findings are given in two of the cases presented. Both show defects of the ventricular septum; in one the defect replaces the membranous septum, in the other the anterior part of the muscular septum is also involved. The pulmonary artery is larger than the aorta and there is right and left ventricular hypertrophy in both specimens. Other changes are minimal.

APICAL DIASTOLIC MURMURS IN PERSISTENT PATENCY OF THE DUCTUS ARTERIOSUS

BY FRANCES GARDNER AND M. ZOOB (*introduced*)

A diastolic murmur was audible at the cardiac apex in 9 patients with patent ductus arteriosus and was recorded phonocardiographically. In 5 patients the murmur could not be distinguished from the diastolic component of the Gibson murmur. In 4 a mid-diastolic murmur, resembling that of mitral stenosis was present, and in two of these the mid-diastolic murmur disappeared after ligation of the ductus, and in a third autopsy showed no stenosis of the mitral valve.

Phonocardiographic evidence suggested that the murmur did not represent transmission of the Gibson murmur to the apex. It was found that the maximum intensity of the Gibson murmur corresponded with the period of relative quiet between the second sound and the mid-diastolic murmur. Furthermore, it was found that respiration produced opposite effects on the two murmurs. The mid-diastolic murmur was increased during inspiration. This would be expected if it were dependent upon flow through the mitral valve. The Gibson murmur was diminished during inspiration.

It is concluded that the murmur belongs to the group of functional mid-diastolic murmurs and that it is not necessarily evidence of mitral stenosis in the presence of patent ductus arteriosus.

An Apparatus for Intermittent Venous Occlusion

By J. Shillingford (*introduced*)

Over ten years have elapsed since Collens and Willensky described their results of the treatment of peripheral vascular disease by intermittent venous occlusion. They showed that this method of treatment was capable of relieving pain, healing ulcers, and increasing walking capacity.

Since this time somewhat conflicting reports have been received as to the value of this method, but there seems little doubt that, clinically, a proportion of patients with peripheral vascular disease are greatly benefited by continued intermittent venous occlusion.

To date, there has not been generally available a simple, and portable, machine suitable for hospital and home use. An apparatus, which will shortly become generally available, has been designed and is now demonstrated. It is small in size, portable, silent in operation, with few moving parts, and can be worked by the patient himself with the minimum of instruction. Any convenient electric light point can be used as its source of power.

Diagnostic Problems in Congenital Cyanotic Heart Disease

By Violet Breakey (*introduced*)

Two cases illustrating diagnostic problems in congenital cyanotic heart disease were discussed in detail:

(1) pure pulmonary stenosis; and
(2) pulmonary tuberculosis occurring in association with the tetralogy of Fallot.

The first case at autopsy showed a stenosis of the pulmonary valve with intact ventricular septum and widely patent foramen ovale. The significant clinical features distinguishing the case from the classical tetralogy of Fallot appeared to be:

(1) The age of onset of cyanosis was much later, i.e. not until five years;
(2) dyspnœa was out of proportion to cyanosis, but attention was drawn to the fact that there were some patients with the tetralogy of Fallot who maintain a relatively high arterial oxygen at rest but rapidly become anoxæmic on the slightest exertion;
(3) cyanosis appeared to vary even more than in the usual tetralogy of Fallot; and
(4) the cardiac contour was strikingly different, with notable fullness of the pulmonary artery and of the right auricle. However, there was not the gross right ventricular enlargement that might be expected.

The choice of surgical procedure in such cases with a tissue-paper thin pulmonary artery was an important matter.

The importance of lung shadows in congenital cyanotic heart disease was mentioned. Rokitansky stated in 1866 that pulmonary tuberculosis and pulmonary stenosis were incompatible. However, textbooks continued to teach that phthisis was a common cause of death in pulmonary stenosis, presumably arguing from the false premise that pulmonary tuberculosis was rarely seen in the vascular lung of mitral stenosis. It seemed now, however, that pulmonary tuberculosis was in fact exceedingly rare in the presence of pulmonary stenosis. In the second case a low pulmonary blood flow consequent on pulmonary stenosis resulted in an unusual picture—a relative absence of toxicity and progression during 12 months in spite of widespread infiltration.

Cardiac Catheterization in Congenital Heart Disease

By G. J. Aitken

The author presented tables illustrating the results obtained from cardiac catheterization in 20 cases of congenital heart disease. The findings agreed with those reported in other series. Particular reference was made to the relative proportion of successful catheterizations of the various cardiac chambers. An unusual course was not infrequent, the most common being into the coronary venous sinus and middle cardiac vein. Such courses were described.

Complications and technical difficulties were discussed. With one exception, venous spasm had been easily controlled. Abnormalities of rhythm were noted in 9 cases. In 8 this took the form of isolated extrasystoles occurring during intracardiac manipulation of the catheter. In the remaining one catheterization initiated a paroxysm of auricular fibrillation, which was terminated by quinidine when early signs of acute congestive failure appeared. Venous thrombosis, apart from a little about the point of entry of the catheter, has not been encountered. In one patient who died of congestive cardiac failure 14 days after catheterization, no evidence of intravascular trauma was detected.

Technical difficulties have been few and wholly concerned with the catheter. It has blocked on three occasions. One catheter was so flexible that control of the tip was not found possible. The outer plastic covering of another, apparently sound on introduction, split completely round its circumference within the lumen of the peripheral vein, during intracardiac manipulation of the tip by rota-

tion of the butt externally. Angled terminal openings in a set of catheters made withdrawal of blood from any venous radicle capricious. Specially ground adaptors have had to be made for some catheters to ensure an air-tight junction between the catheter and the syringe.

With suitable catheters and average skill, no technical difficulty need be anticipated in performing cardiac catheterization. An occasional failure is to be expected from a persistently abnormal catheter course. The danger of precipitation of a cardiac arrhythmia is real.

Cardiac Infarction with Pain Confined to Effort

By A. Morgan Jones and E. J. Wade

The authors have reviewed 98 consecutive cases of angina of effort. Eight have died or can not be traced; 90 have been re-interviewed to ascertain whether there has ever been any clinical episode suggestive of infarction. In 62 cases the pain was typical in every respect of angina of effort, being confined to exertion, invariably relieved by rest, and never lasting more than 15 minutes. Unless there was unequivocal evidence of infarction in the routine electrocardiograms, a full electrocardiographic investigation was made, including standard leads, unipolar limb leads, 6 unipolar præcordial leads, and 6 high unipolar præcordial leads. Infarction was diagnosed when two of the following changes were present in leads facing ventricular muscle: (1) typical QRS changes; (2) S–T changes; (3) T wave changes not explicable by ventricular enlargement. T wave changes alone were not accepted as proof of infarction.

In the 62 selected cases typical changes of cardiac infarction were present in 17 (28 per cent), and abnormal electrocardiograms suggestive of infarction were found in 12 (19 per cent). Abnormal cardiograms, not suggestive of infarction, were present in 5 cases (8 per cent), and in 28 cases (45 per cent) the cardiogram was within normal limits.

Coronary Attacks in General Practice

By C. Papp

Coronary attack is a clinical term for persistent anginal pain, lasting half an hour or more, arising at rest and unresponsive to trinitrin.

Twenty-seven patients seen in general practice and treated for coronary attacks were investigated; according to the gravity of the clinical symptoms and blood sedimentation rate (B.S.R.), they were divided into three groups, of slight, moderate, and severe coronary attacks. Electrocardiography was used for diagnosis but disregarded for assessment. It confirmed recent myocardial ischæmia in 20, and was inconclusive in 5; no records were obtained in 2 patients who died early.

Slight coronary attack. 12 cases, no death; 7 confirmed, 5 unconfirmed by electrocardiogram; this latter group includes 4 with severe hypertension (3 women) and one with Buerger's disease. Pain was moderate, and relieved by single injection of morphia gr. $\frac{1}{4}$–$\frac{1}{2}$ and rarely recurred. The fall of blood pressure was short-lived and slight. Pyrexia was present only in a few. The B.S.R. was either normal from the onset or went back to normal within a fortnight. Shock and pulmonary congestion were absent and so were cardiac signs except for occasional ectopic rhythm during the attack.

Moderate coronary attack. 5 cases, none fatal, and all confirmed by electrocardiogram. Pain was severe, and repeated injections of morphia were often required (total amount gr. $\frac{1}{2}$–$\frac{3}{4}$). Pain often recurred in a slighter form after the attack. Shock was slight or moderate, always relieved by morphia and never lasting longer than the pain. Blood pressure might fall considerably and return to normal only after a fortnight or more. Pyrexia was present for a few days. B.S.R. was back to normal at the end of three to four weeks. Cardiac and pulmonary signs were absent.

Severe coronary attack. 10 cases; of these 7 died. Pain was often in three phases. The main attack was preceded by a slight coronary attack, often in the form of short and repeated attacks of angina at rest, responding to trinitrin. Rest in bed did not prevent the second phase, the main attack, which was characterized by extreme pain or by pain of 24 to 48 hours' duration. This was relieved by intravenous and subcutaneous morphia (total amount gr. $\frac{3}{4}$–1 with added atropine). The third phase, consisting of further attacks requiring morphia, often followed and was fatal in 3. Shock, severe and protracted (fatal in 4), was the leading symptom in this group; it produced fall of blood pressure to dangerous levels and permanent lowering in those who recovered; it was also responsible for pulmonary congestion and the high incidence of heart failure (5 cases). Pyrexia was high after shock had subsided. The return to normal of the B.S.R. was delayed by pulmonary complications. Cardiac signs such as persistently high pulse rate, triple rhythm, and apical systolic murmurs were precursors of congestive heart failure. Death was due to shock (4 cases), congestive heart failure (1 case), pulmonary embolus (1 case probable), and to coronary attack during sleep (1 case probable). Death

from shock occurred within hours, from congestive heart failure within months, or from further coronary attack at any time; the last could not be foretold by the electrocardiograph.

Electrocardiographic signs were in broad agreement with clinical signs. In slight and moderate coronary attacks temporary or definite inversion of T in one or more leads was found. In severe coronary attacks, current of injury, Q waves, and later deep inversion of T were the prominent features. In a few discordant cases, clinical signs proved of greater prognostic value than the electrocardiogram.

Treatment was adapted to gravity. Slight and moderate coronary attacks required symptomatic treatment only. Rest in bed was reduced to two weeks in the slight and to three or four weeks in the moderate group, according to the return to normal of the B.S.R. Angina of effort was not provoked by the shorter rest and could not be prevented by extension of rest. The prognosis in slight and moderate coronary attack was favourable, and 16 out of 17 patients were active in profession, business, or household. In severe coronary attacks shock needed active treatment; oxygen tent might be life-saving and anti-coagulant treatment was a necessity, particularly if pulmonary complications were present. Dicoumarol was not used because of its dangers; heparin was safe without laboratory control. Intravenous theophylline-ethylene-diamine combined with ouabaine or oral digitalis was used at the first signs of failure. Recovery from a severe coronary attack was uncommon over the age of 60; those who survived in this series were of the younger age group, and only one of the three recovered without residual cardiac damage.

The Radiology of Heart Failure Due to Cardiac Infarction

By Frederick Jackson (*introduced*)

Teleradiograms were taken before and after treatment in 8 cases of heart failure following cardiac infarction without hypertension. In 4 the heart was only slightly enlarged during failure. In the other 4 it was moderately enlarged, but returned almost to normal size with treatment in 2; hydropericardium was suspected in these and confirmed once at necropsy. The enlargement persisted in the other 2 cases.

The special features of this variety of failure are these. It may occur in a heart that is almost normal in size. During failure the heart usually enlarges, but not greatly, and it may scarcely enlarge at all. With treatment the heart may return very nearly to normal size. The enlargement may be due to hydropericardium, as was shown once post mortem. Raising of the diaphragm, pulmonary congestion, and hydrothorax are usual. They may develop or largely disappear in as short a time as one week, but generally take longer.

Non-rheumatic Interstitial Myocarditis

By Florence McKeown (*introduced*)

The incidence of interstitial myocarditis has been investigated in routine post-mortem material. It was found to be present in 2 per cent of cases. There was a tendency for it to occur in association with certain infections with some frequency, and it has been observed in pneumonia, meningococcal septicæmia, diphtheria, and miliary tuberculosis.

The author discussed its relative importance in these conditions. A further group of isolated myocarditis was included, in which it was impossible to establish a correlation with any existing infection.

Some Characteristics of Instruments Designed for Recording Electrocardiograms and Heart Sounds

By A. Morgan Jones and M. G. Saunders (*introduced*)

The determination and importance of the range of frequency response and of the duration of the time constant in electrocardiographs and cardiophonographs were discussed and illustrated by the characteristics of certain commercial recorders.

The Phonocardiogram of Aortic Stenosis

By A. Leatham

Aortic stenosis produces a murmur of characteristic shape in the phonocardiogram both in the aortic and in the mitral areas. It often starts late in relation to the electrocardiogram and finishes well before the second sound, but sounds have high-frequency components simulating murmurs and it may be difficult to tell where one ceases and the other begins. In each of 20 subjects with aortic stenosis but without evidence of mitral valvular disease, the systolic murmur was small at its onset and rose to a peak in mid-systole, then diminished in size until it was small or absent at the second sound. Though the mid-systolic accentuation was greatest in the aortic area it was always present in the mitral area. In most cases the second sound was followed by an early diastolic murmur.

In mitral valvular disease the systolic murmur was earlier and reached the second sound; there was no sharp mid-systolic accentuation.

In a group of some 20 cases of pulmonary stenosis there was also a mid-systolic accentuation, but it was seldom so great as in aortic stenosis and the murmur usually reached the second sound.

The phonocardiogram of aortic stenosis may prove of value in clinical diagnosis when the systolic murmur is loud at the apex. The shape described was found in all cases of aortic stenosis so far examined and was different from the shape in mitral valvular disease. Whether it is truly distinctive or whether it may be simulated in some other condition remains to be determined.

Examination of the Heart at Necropsy

By J. Shillingford (*introduced*)

A closer examination of the heart at necropsy than the one usually carried out has been developed at the London Hospital during the past year.

The coronary arteries are injected with a radio-opaque substance, and an apparatus has been designed to facilitate this technique as a routine method of examination. The correlation between filling defects as shown on the X-ray and arterial lesions has been studied.

Cardiac chamber volume has been measured by means of wax casts, and a simple method of making these has been found. Hypertrophy of the muscle wall is shown by multiple measurements and a standard for normals has been established.

For the most part, the examination has been developed to correlate autopsy findings with those in life as shown by the multiple chest lead electrocardiogram.

ABSTRACTS OF CARDIOLOGY

Asymptomatic Heart Disease: Observations Made during the Early Recruiting Period for Navy and Marine Enlistments. A. S. HYMAN. *Amer. J. Med.* **5**, 351–364, Sept., 1948.

Of 1900 boys and men examined before enlistment in the Navy or Marine Corps and referred to a cardiovascular specialist 350 were found to be suffering from some form of asymptomatic cardiovascular disease, as regards which the history was entirely negative. The ages varied between 17 and 51, average 26; the smallest age groups were those of 47, 49, 50, and 51 years with 3 cases each. Valvular heart disease was found in 169 (mitral insufficiency 93, mitral stenosis 41, aortic incompetence 22, aortic stenosis 9, congenital lesions 4), and hypertension in 89 (systolic pressure 150 to 170 mm. Hg., 58; 170 to 190 mm., 25; 190 to 210 mm., 5; 210 to 220 mm., 1). It is emphasized that high blood pressure may develop without giving rise to any symptoms and that pathological signs start to develop with pressures exceeding 170 mm. Hg. Arrhythmias were present in 55 (ventricular extrasystoles 18, auricular 6, nodal 2, and bifocal 1; tachycardia of or exceeding 110, 19; auricular fibrillation 6; complete heart block 2; and incomplete heart block 1). Cardiac hypertrophy was found in 26, of whom 22 had engaged in athletics (15 in more than moderate degree). This was the most common single factor found in this group. Premature arterial changes were found in 11. Only those in the group with premature contractions and 4 amongst the 26 with cardiac hypertrophy were accepted for service. The explanation for the absence of symptoms in these conditions in the examined group is discussed.

A. Schott

Arterial Blood Pressure in Labour and the Puerperium. D. Y. DARON. *Akush. Ginek.*, No. 5, 10–13, 1948.

The variations in the blood pressure during normal labour were studied in 45 women. Systolic pressure in 37 at the beginning of labour was between 105 and 125 mm. Hg., varying in the remainder from 130 to 155 mm. During the first stage, systolic pressure tended to be higher in primiparæ and younger women. During the second stage, contrary to expectation, systolic pressure changed little, save in rapid labours. In most cases the systolic pressure rose in the third stage (in 30 by 15 mm., in 7 by 20 to 40 mm.); this rise was most marked in rapid labours and in younger women. After placental expulsion, systolic pressure returned in 36 forthwith to normal, return being slower after longer labours.

Diastolic pressure in 35 women exceeded 70 mm. Hg. at the onset of labour. During the second stage in most cases it either rose by 10 to 20 mm. or remained unchanged. During the third stage it rose still further, only to fall again in most cases after expulsion of the placenta. Diastolic pressure was highest in older women and in more rapid labours. When labour was prolonged there was usually a sharp rise soon after expulsion of the fœtus.

Changes in the character of the pulse are described. The work of the heart was also studied by the use of Lilienstrand coefficient. The cardiovascular system was not subjected to undue stress in either the first or the second stage, the greatest burden being placed on it after expulsion of the fœtus by the sudden alteration in intra-abdominal pressure.

S. S. B. Gilder

An Analysis of Certain Factors Associated with the Production of Experimental Dissection of the Aortic Media, in Relation to the Pathogenesis of Dissecting Aneurysm. J. S. ROBERTSON and K. V. SMITH. *J. Path. Bact.*, **60**, 43–49, Jan., 1948.

The pressure required to produce experimental dissection of the aorta by forcing water through a needle into the media was measured in 42 adults of different ages and both sexes. In all cases this pressure was far higher than the blood pressure, even in severe hypertension. These results (which were well analysed statistically) support the view that aortic dissection only occurs in cases of marked medial degeneration.

D. M. Pryce

Thrombosis as a Factor in the Pathogenesis of Aortic Atherosclerosis. J. B. DUGUID. *J. Path. Bact.* **60**, 57–61, Jan., 1948.

Recent thrombotic deposits were found in the aorta in 19 of 50 cases post-mortem. Whilst most frequent over atheromatous ulcers of older subjects they were also found in association with early atheromatous streaks and even where the wall appeared normal. Often the deposits were superimposed on earlier deposits. Transitional appearances indicated that the deposits were gradually transformed into intimal thickenings, which would ordinarily have been regarded as purely arteriosclerotic. The author has previously shown the importance of this process in the coronary arteries.

D. M. Pryce

The Application of Oximetry and Cardiac Catheterization to the Diagnosis of Congenital Heart Disease. H. B. BURCHELL. *J. Iowa med. Soc.*, **38**, 364–368, Aug., 1948.

The diagnosis of congenital heart disease by the traditional methods is notoriously difficult. Apart from those cases with such typical features as the murmurs of a patent ductus arteriosus and the tremendous pulsa-

tions of the hilar vessels in atrial septal defect, so-called pathognomonic signs are rare. The author describes the use of the cardiac catheter together with a photoelectric oximeter in the investigation of these cases. The oximeter permits recognition of degrees of unsaturation of arterial blood with oxygen which are insufficient to cause recognizable cyanosis. In Fallot's tetralogy the degree of pulmonary stenosis may be estimated by the extent of the fall in arterial oxygen saturation during exercise. In the most severe cases this may fall as low as 20%. Those patients who cannot maintain an arterial saturation of at least 70% at complete rest are in a very precarious condition.

Catheterization of the heart involves accurate radiological studies of: (1) the position of the catheter tip, together with observations on (2) intracardiac pressure, and (3) variations in oxygen saturation of the blood in the various positions. Without all these it is impossible to decide the exact location of the catheter tip within the heart owing to the great deviations from normal pressures which may take place in the presence of complex congenital defects. The oximeter may be used for rapid determination of oxygen saturation of any sample of blood withdrawn through the catheter. Pressures within the heart are recorded with sufficient accuracy for clinical purposes by means of strain-gauge manometers.

The recognition of an atrial septal defect is one of the easiest examples of the use of this method. Its presence may be determined by the ease of passage of the catheter through the defect into the left auricle or pulmonary veins, and also by the finding of arterialized blood in the right atrium. Similarly, arterialization of blood in the pulmonary artery is practically diagnostic of patent ductus arteriosus. High right intraventricular pressures with normal pulmonary artery pressures are always suggestive of pulmonary stenosis. The author points out that the calculations used by Bing for the assessment of pulmonary blood flow and other factors need further critical re-evaluation on account of various inaccuracies which may arise in the techniques used. He also points out that the clinical features of the various congenital lesions often permit of diagnosis with fair certainty, and cardiac catheterization is of most value in atypical cases. Angiocardiography is also of immense value in the study of such problem cases. *J. McMichael*

Hoarseness in Heart Disease. J. L. THOMPSON and A. D. KISTIN. *Ann. intern. Med.*, **29**, 259–273, Aug., 1948.

The authors were able to find only 30 reported cases of left recurrent laryngeal nerve palsy associated with heart disease in which necropsy findings were recorded. Dilatation of the pulmonary artery was the prime cause of the nerve injury. They describe 2 cases of their own in which the sole initial complaint was hoarseness.

The literature is reviewed at some length, and the various explanations of the ætiology are given. It had been suggested that the combination of heart disease and recurrent laryngeal paralysis is so infrequent that their association is purely coincidental; many cases remain unexplained. In mitral stenosis paralysis of the nerve has been found ten times as often as in hospital patients in general, and, were the association coincidental, the right and the left nerve ought to be equally affected. No case is recorded of paralysis of the right nerve alone, and where both nerves were held to be affected there has been no necropsy. Attempts have been made to link the paralysis with the presence of the ligamentum arteriosum as it passes backwards from the left pulmonary artery to the aorta, but the evidence is contradictory. In most of the cases studied pulmonary artery dilatation was a common factor, but the fact remains that, while such dilatation is frequent, associated laryngeal nerve paralysis is rare.

Case I is illustrated by a skiagram of the right oblique view with barium-filled œsophagus, photomicrographs, and photographs of the dissection. In these photographs the anatomical relations of the various parts are seen with clarity. In Case II the angiocardiograms are reproduced with explanatory diagrams. *Donald Hall*

The Effect of Exercise on the Electrocardiogram [Master "Two-step" Test] in the Diagnosis of Coronary Insufficiency. D. UNTERMAN and A. C. DEGRAFF. *Amer. J. med. Sci.*, **215**, 671–685, June, 1948.

A standard two-step exercise test (Master, *Amer. J. med. Sci.*, 1929, **177**, 223) was used and electrocardiograms (leads I, II, III, and CF4) were taken as quickly as possible afterwards. The criteria for a positive test, which were adopted as more marked than the changes seen in 31 normal controls, were as follows: (1) A depression of the RS–T junction of more than 1 mm. in the standard leads or more than 0·75 mm. in CF4, this lead being standardized at half the usual sensitivity. (2) Conversion of an upright T wave to an isoelectric or inverted T wave in leads I, II, or CF4 or of a diphasic or inverted T to upright.

The test was tried in 91 patients with various forms of heart disease, with positive results in 31. Positive results were obtained in 48% of patients with typical angina, 24% of those with atypical symptoms, and in 28% of those without pain. Ten patients experienced anginal pain during the exercise and in 7 of these the test was positive. The influence of food, digitalis, and recent acute illness is also considered.

[The control group in this series consisted of younger patients than those with heart disease. The patients with heart disease are classified on an ætiological basis only, so that the possible influence of cardiac enlargement or failure cannot be determined.] *J. W. Litchfield*

The Immediate Sequelae of Myocardial Infarction. Their Relation to the Prognosis. A. SELZER. *Amer. J. med. Sci.*, **216**, 172–178, Aug., 1948.

A study of 130 cases of recent myocardial infarction coming to necropsy was made in an effort to determine the immediate cause of death. In 35 the patient was previously so ill that the myocardial infarction might be regarded as a terminal event. In the other 95 there was little limitation of activities before the infarction. These

patients were divisible into four groups. In the first, consisting of 28 patients, death was due to progressive circulatory failure, with or without shock. The 24 patients in the second group died suddenly 24 hours or more after the infarction and presumably from a fatal arrhythmia. In the third group were 32 patients who died as the result of some complication demonstrable at necropsy—rupture of the ventricle (8), embolic phenomena (15); the other complications were not directly connected with the infarction. The remaining 11 patients died of miscellaneous causes—recurrent coronary occlusion (5), prolonged illness for which no cause could be found (4), and possibly digitalis poisoning (2). No correlation was found between the age of the patient, the severity of coronary arteriosclerosis, the size of the infarct, the presence of old scars or cardiac hypertrophy, the course and duration of the illness or the frequency of complications. Thus, a considerable number of patients with myocardial infarction die, not from cardiac insufficiency, but from serious arrhythmias, thrombo-embolic phenomena, and shock. *C. Bruce Perry*

Electrocardiographic Changes in Diphtheria. S. S. ALTSHULER, K. M. HOFFMAN, and P. J. FITZGERALD. *Ann. intern. Med.*, **29**, 294–305, Aug., 1948.

This is a study of 600 patients in the American Occupied Zone of Germany between September, 1945, and December, 1946. All the cases reported were confirmed bacteriologically, 26 being examples of cutaneous diphtheria. The average age of the patients was 23 years and 37 were females. An electrocardiogram was taken as soon as diphtheria was suspected clinically or a positive culture obtained, thereafter weekly or more often if thought necessary. Those with severe or prolonged cardiographic changes were invariably returned to the U.S.A. for convalescence. The period of observation for patients with cardiographic changes varied between 8 and 23 weeks.

Of the 600 patients 143 (24%) presented cardiographic changes at some time during their stay in hospital. By far the most common abnormality was low voltage or negativity of the T wave in two or more leads (108 cases); next in frequency, but far behind, was prolongation of the P–R interval (11 cases) and depression of ST segments in two or more leads (10 cases). All cardiograms were checked independently and no borderline curves were included. Of the T wave changes 30 involved leads II and III, 28 all four leads, and 25 leads I, II, and III. Slight slurring and splintering of the QRS segment were common, but significant prolongation was seen only in the 2 patients with right bundle branch block. Low voltage of QRS in all leads was present in 3 patients only. Electrocardiographic changes were met with for the first time after the fourth week only in 5 of the 600 patients examined. [The authors state that " patients with persistent abnormalities in all leads usually had manifested clinically severe infections " but in the summary " severity of clinical infection and severity and duration of electrocardiographic changes in diphtheria cannot be correlated."] It is pointed out that this study does not support the view that prolongation of the P–R interval is the most common abnormality in diphtheria.

The two patients with heart block had been treated for hæmolytic streptococcal sore throat and discharged, completely asymptomatic, to duty within the week. One was readmitted in 6 days, the other in 8, both in cardiovascular collapse. In the 2 fatal cases T waves were negative in all leads. In 4 patients phasic alternation between normal and abnormal electrocardiograms was found.

The paper is well illustrated by serial cardiograms, and the authors consider that in diphtheria, alike in the acute stage and in convalescence, the electrocardiogram is essential to the evaluation of the physical state of the patient. *Donald Hall*

Dicumarol in Experimental Myocardial Infarction. G. V. LEROY and L. A. NALEFSKI. *J. Lab. clin. Med.*, **33**, 961–971, Aug., 1948.

At first dicoumarol was used only for patients who had already experienced thrombo-embolic complications of cardiac infarction—either repeated episodes of multiple thrombosis in different areas of the coronary tree or repeated phenomena elsewhere, for example, in the lungs. Later it was given purely prophylactically against such complications.

The incidence of thrombo-embolic complications in recent myocardial infarction is difficult to determine, as the data are conflicting: the figures given by different authors vary from 9·9 to 45%. Even the incidence of mural thrombosis of the endocardium is difficult to ascertain, being stated variously as between 17 and 83%. However, it is evident that thrombo-embolism is an important complication of myocardial infarction. The authors state that in all the reports of results of anticoagulant therapy there has been an apparently significant reduction in the number of thrombo-embolic complications and in the general mortality rate, but they point out that there has been as yet no report which includes suitable controls.

The chief hazard with anticoagulant therapy is the development of a hæmorrhagic state and it is essential that treatment be controlled by prothrombin determinations. As the early stage of infarction is characterized by hyperæmia and hæmorrhage the authors thought it possible that the use of anticoagulants might accentuate the hæmorrhagic stage and thus prolong resolution of the infarct. Myocardial infarction was produced in 25 dogs by ligation of the anterior descending branch of the left coronary artery. Fifteen were given dicoumarol in amounts similar to those used in the treatment of patients with recent infarction. The animals were killed at intervals of 5 to 22 days. There were slight differences between the control group and the dicoumarol-treated group, but the authors state that there was no evidence that the altered coagulability of the blood affected the extent or healing of infarcts. Serial electrocardiograms showed no significant difference between treated animals and controls. No deleterious influence on healing was demonstrated. *S. Oram*

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